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LOGINID:SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * * * Welcome to STN International * * * * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 28 PATDPAFULL - New display fields provide for legal status
data from INPADOC
NEWS 4 FEB 28 BABS - Current-awareness alerts (SDIs) available
NEWS 5 MAR 02 GBFULL: New full-text patent database on STN
NEWS 6 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 7 MAR 03 MEDLINE file segment of TOXCENTER reloaded
NEWS 8 MAR 22 KOREPAT now updated monthly; patent information enhanced
NEWS 9 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 10 MAR 22 PATDPASPC - New patent database available
NEWS 11 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 12 APR 04 EPFULL enhanced with additional patent information and new
fields
NEWS 13 APR 04 EMBASE - Database reloaded and enhanced
NEWS 14 APR 18 New CAS Information Use Policies available online
NEWS 15 APR 25 Patent searching, including current-awareness alerts (SDIs),
based on application date in CA/Caplus and USPATFULL/USPAT2
may be affected by a change in filing date for U.S.
applications.
NEWS 16 APR 28 Improved searching of U.S. Patent Classifications for
U.S. patent records in CA/Caplus
NEWS 17 MAY 23 GBFULL enhanced with patent drawing images
NEWS 18 MAY 23 REGISTRY has been enhanced with source information from
CHEMCATS
NEWS 19 JUN 06 The Analysis Edition of STN Express with Discover!
(Version 8.0 for Windows) now available
NEWS 20 JUN 13 RUSSIAPAT: New full-text patent database on STN
NEWS 21 JUN 13 FRFULL enhanced with patent drawing images
NEWS 22 JUN 27 MARPAT displays enhanced with expanded G-group definitions
and text labels
NEWS 23 JUL 01 MEDICONF removed from STN
NEWS 24 JUL 07 STN Patent Forums to be held in July 2005
NEWS 25 JUL 13 SCISEARCH reloaded
NEWS 26 JUL 20 Powerful new interactive analysis and visualization software,
STN AnaVist, now available

NEWS EXPRESS JUNE 13 CURRENT WINDOWS VERSION IS V8.0, CURRENT
MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS INTER General Internet Information
NEWS LOGIN Welcome Banner and News Items
NEWS PHONE Direct Dial and Telecommunication Network Access to STN
NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 16:27:28 ON 10 AUG 2005

```
=> file registry
COST IN U.S. DOLLARS                               SINCE FILE      TOTAL
                                                ENTRY        SESSION
FULL ESTIMATED COST                           0.21          0.21
```

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005
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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2005 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 9 AUG 2005 HIGHEST RN 859282-03-4
DICTIONARY FILE UPDATES: 9 AUG 2005 HIGHEST RN 859282-03-4

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

```
*****
*   * The CA roles and document type information have been removed from *
*   * the IDE default display format and the ED field has been added,    *
*   * effective March 20, 2005. A new display format, IDERL, is now      *
*   * available and contains the CA role and document type information. *
*   *
*****
```

Structure search iteration limits have been increased. See HELP SLIMITS for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
<http://www.cas.org/ONLINE/DBSS/registryss.html>

```

=> E "4-HYDROXYTAMOXIFEN"/CN 25
E1          1   4-HYDROXYSTYRYL PHENYL KETONE POTASSIUM SALT/CN
E2          1   4-HYDROXYTACRINE/CN
E3          1 --> 4-HYDROXYTAMOXIFEN/CN
E4          1   4-HYDROXYTAMOXIFEN ACID/CN
E5          1   4-HYDROXYTECOMANINE/CN
E6          1   4-HYDROXYTESTOSTERONE/CN
E7          1   4-HYDROXYTESTOSTERONE_17-HEMISUCCINATE/CN

```

E8 1 4-HYDROXYTESTOSTERONE 17-TERT-BUTYLDIMETHYLSILYL ETHER/CN
E9 1 4-HYDROXYTESTOSTERONE 4-HEMIGLUTARATE/CN
E10 1 4-HYDROXYTESTOSTERONE 4-HEMISUCCINATE/CN
E11 1 4-HYDROXYTESTRACHLOROBENZONITRILE/CN
E12 1 4-HYDROXYTETRACHLOROPYRIDINE/CN
E13 1 4-HYDROXYTETRACYCLOXIDE/CN
E14 1 4-HYDROXYTETRADECANE/CN
E15 1 4-HYDROXYTETRAFLUOROBENZOIC ACID/CN
E16 1 4-HYDROXYTETRAFLUOROBENZOIC ACID 1-METHYLHEPTYL ESTER/CN
E17 1 4-HYDROXYTETRAFLUOROBENZOIC ACID OCTYL ESTER/CN
E18 1 4-HYDROXYTETRAFLUOROPYRIDINE/CN
E19 1 4-HYDROXYTETRAFLUOROPYRIDINE POTASSIUM SALT/CN
E20 1 4-HYDROXYTETRAFLUOROPYRIDINE SODIUM SALT/CN
E21 1 4-HYDROXYTETRAHYDRO-2H-PYRAN/CN
E22 1 4-HYDROXYTETRAHYDRO-3-FURANYL NITRITE/CN
E23 1 4-HYDROXYTETRAHYDROFURAN-2,4-DIMETHANOL/CN
E24 1 4-HYDROXYTETRAHYDROFURAN-2-METHANOL/CN
E25 1 4-HYDROXYTETRAHYDROPYRAN/CN

=> S E3
L1 1 4-HYDROXYTAMOXIFEN/CN

=> DIS L1 1 SQIDE
THE ESTIMATED COST FOR THIS REQUEST IS 6.15 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L1 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2005 ACS on STN
RN 68047-06-3 REGISTRY
CN Phenol, 4-[{1Z}-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-
(9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Phenol, 4-[1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]-,
(Z)-
OTHER NAMES:
CN (Z)-4-Hydroxytamoxifen
CN 4-Hydroxytamoxifen
CN 4-[{1Z}-1-[4-[2-(dimethylamino)ethoxy]phenyl]-2-phenyl-1-butenyl]phenol
CN Hydroxytamoxifen
CN ICI 79280
CN trans-4-Hydroxytamoxifen
CN trans-Hydroxytamoxifen
FS STEREOSEARCH
DR 65213-48-1, 72732-26-4, 76276-99-8
MF C26 H29 N O2
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS,
BIOTECHNO, CA, CAPLUS, CASREACT, CEN, CHEMCATS, CIN, CSCHEM, DDFU,
DRUGU, EMBASE, IMSDRUGNEWS, IPA, NIOSHTIC, PHAR, PROMT, RTECS*,
TOXCENTER, USPAT2, USPATFULL
(*File contains numerically searchable property data)
DT.CA Caplus document type: Conference; Dissertation; Journal; Patent
RL.P Roles from patents: ANST (Analytical study); BIOL (Biological study);
FORM (Formation, nonpreparative); PREP (Preparation); PROC (Process);
PRP (Properties); RACT (Reactant or reagent); USES (Uses)
RL.DP Roles for non-specific derivatives from patents: BIOL (Biological
study); PREP (Preparation); PROC (Process); USES (Uses)
RL.NP Roles from non-patents: ANST (Analytical study); BIOL (Biological
study); FORM (Formation, nonpreparative); OCCU (Occurrence); PREP
(Preparation); PROC (Process); PRP (Properties); RACT (Reactant or
reagent); USES (Uses)
RL.DNP Roles for non-specific derivatives from non-patents: ANST (Analytical
study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation);

```
PROC (Process); PRP (Properties); USES (Uses)
Double bond geometry as shown.

/ Structure 1 in file .gra /
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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**
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```
1268 REFERENCES IN FILE CA (1907 TO DATE)
 35 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1273 REFERENCES IN FILE CAPLUS (1907 TO DATE)
```

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=> file medline
COST IN U.S. DOLLARS          SINCE FILE      TOTAL
                                ENTRY        SESSION
FULL ESTIMATED COST          7.30          7.51
```

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FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005
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FILE LAST UPDATED: 9 AUG 2005 (20050809/UP). FILE COVERS 1950 TO DATE.
```

On December 19, 2004, the 2005 MeSH terms were loaded.

The MEDLINE reload for 2005 is now available. For details enter HELP RLOAD at an arrow prompt (=>). See also:

```
http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04\_mesh.html
```

OLDMEDLINE now back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2005 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s 11
L2          0 L1

=> s 4-HYDROXYTAMOXIFEN/CN
L3          666 4-HYDROXYTAMOXIFEN/CN (10 TERMS)
          ("4-HYDROXYTAMOXIFEN"+XUSE/CN)

=> s breast or mammar?
    197959 BREAST
    3409 BREASTS
    198389 BREAST
          (BREAST OR BREASTS)
    54038 MAMMAR?
L4          233739 BREAST OR MAMMAR?

=> s density
    243455 DENSITY
    24925 DENSITIES
L5          256821 DENSITY
          (DENSITY OR DENSITIES)

=> s 15 (S) 14
L6          1500 L5 (S) L4
```

=> s 16 and 13
L7 2 L6 AND L3

=> d ibib 1-2

L7 ANSWER 1 OF 2 MEDLINE on STN
ACCESSION NUMBER: 84155068 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6671136
TITLE: Interaction of [3H] estradiol - and [3H]
monohydroxytamoxifen-estrogen receptor complexes with a
monoclonal antibody.
AUTHOR: Tate A C; DeSombre E R; Greene G L; Jensen E V; Jordan V C
CONTRACT NUMBER: P30-CA-14520 (NCI)
SOURCE: Breast cancer research and treatment, (1983) 3 (3) 267-77.
Journal code: 8111104. ISSN: 0167-6806.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198405
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840502

L7 ANSWER 2 OF 2 MEDLINE on STN
ACCESSION NUMBER: 84106548 MEDLINE
DOCUMENT NUMBER: PubMed ID: 6692388
TITLE: Differences between estrogen- and antiestrogen-estrogen
receptor complexes from human breast tumors identified with
an antibody raised against the estrogen receptor.
AUTHOR: Tate A C; Greene G L; DeSombre E R; Jensen E V; Jordan V C
CONTRACT NUMBER: P30-CA-14520 (NCI)
SOURCE: Cancer research, (1984 Mar) 44 (3) 1012-8.
Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198403
ENTRY DATE: Entered STN: 19900319
Last Updated on STN: 19970203
Entered Medline: 19840323

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
1.50 9.01

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005
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FILE COVERS 1907 - 10 Aug 2005 VOL 143 ISS 7
FILE LAST UPDATED: 9 Aug 2005 (20050809/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 4-HYDROXYTAMOXIFEN/CN
REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L9 1273 L8

=> s breast or mammar?
62426 BREAST
523 BREASTS
62610 BREAST
(BREAST OR BREASTS)
77390 MAMMAR?

L10 101462 BREAST OR MAMMAR?

=> s density
269024 DENSITY
114999 DENSITIES
L11 358546 DENSITY
(DENSITY OR DENSITIES)

=> s l10 (S) l11
L12 235 L10 (S) L11

=> s l12 and 19
L13 1 L12 AND L9

=> s dens?
L14 496119 DENS?

=> s l14 and l10
L15 949 L14 AND L10

=> s l15 and 19
L16 3 L15 AND L9

=> d ibib 1-3

L16 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:531338 CAPLUS
DOCUMENT NUMBER: 141:65145
TITLE: Reduction of breast density with
4-hydroxy tamoxifen
INVENTOR(S): Bua, Jay
PATENT ASSIGNEE(S): Laboratoires Besins International, Fr.

SOURCE: PCT Int. Appl., 31 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004054558 | A2 | 20040701 | WO 2003-EP15030 | 20031215 |
| WO 2004054558 | A3 | 20041028 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004138314 | A1 | 20040715 | US 2003-734644 | 20031215 |
| PRIORITY APPLN. INFO.: | | | US 2002-433958P | P 20021218 |

L16 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1985:558391 CAPLUS
 DOCUMENT NUMBER: 103:158391
 TITLE: Selection and characterization of a breast cancer cell line resistant to the antiestrogen LY 117018
 AUTHOR(S): Bronzert, Diane A.; Greene, Geoffrey L.; Lippman, Marc E.
 CORPORATE SOURCE: Med. Branch, Natl. Cancer Inst., Bethesda, MD, 20205, USA
 SOURCE: Endocrinology (1985), 117(4), 1409-17
 DOCUMENT TYPE: CODEN: ENDOAO; ISSN: 0013-7227
 LANGUAGE: Journal English

L16 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1985:481986 CAPLUS
 DOCUMENT NUMBER: 103:81986
 TITLE: Characterization of the subunit nature of nuclear estrogen receptors by chemical cross-linking and dense amino acid labeling
 AUTHOR(S): Miller, Margaret Ann; Mullick, Alaka; Greene, Geoffrey L.; Katzenellenbogen, Benita S.
 CORPORATE SOURCE: Dep. Physiol. Biophys., Univ. Illinois, Urbana, IL, 61801, USA
 SOURCE: Endocrinology (1985), 117(2), 515-22
 DOCUMENT TYPE: CODEN: ENDOAO; ISSN: 0013-7227
 LANGUAGE: Journal English

=> d his

(FILE 'HOME' ENTERED AT 16:27:28 ON 10 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005

E "4-HYDROXYTAMOXIFEN"/CN 25

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005
L2 0 S L1
L3 666 S 4-HYDROXYTAMOXIFEN/CN
L4 233739 S BREAST OR MAMMAR?
L5 256821 S DENSITY
L6 1500 S L5 (S) L4
L7 2 S L6 AND L3

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005
S 4-HYDROXYTAMOXIFEN/CN

FILE 'REGISTRY' ENTERED AT 16:30:42 ON 10 AUG 2005
L8 1 S 4-HYDROXYTAMOXIFEN/CN

FILE 'CAPLUS' ENTERED AT 16:30:43 ON 10 AUG 2005
L9 1273 S L8
L10 101462 S BREAST OR MAMMAR?
L11 358546 S DENSITY
L12 235 S L10 (S) L11
L13 1 S L12 AND L9
L14 496119 S DENS?
L15 949 S L14 AND L10
L16 3 S L15 AND L9

=> s cancer? or tumor? or neoplas?
265968 CANCER?
398752 TUMOR?
417935 NEOPLAS?

L17 659727 CANCER? OR TUMOR? OR NEOPLAS?

=> s l17 and l10
L18 73400 L17 AND L10

=> s l18 (S) l10
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'L18 (S) L10'
L19 73400 L18 (S) L10

=> s l17 (S) l10
L20 69226 L17 (S) L10

=> s l20 and l18
1273 L8
L21 493 L20 AND L8

=> s l21 and percutan?
8318 PERCUTAN?
L22 4 L21 AND PERCUTAN?

=> d ibib 1-22

L22 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:857374 CAPLUS
DOCUMENT NUMBER: 141:325697
TITLE: Prevention and treatment of breast
 cancer with 4-hydroxytamoxifen
INVENTOR(S): Salin-Drouin, Dominique; Wepierre, Jacques; Rouanet,
 Philippe
PATENT ASSIGNEE(S): Laboratoires Besins International, Fr.
SOURCE: PCT Int. Appl., 46 pp.
CODEN: PIXDZ

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|--|-----------------|------------|
| WO 2004087123 | A1 | 20041014 | WO 2003-EP15029 | 20031215 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BG, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005031695 | A1 | 20050210 | US 2003-734638 | 20031215 |
| PRIORITY APPLN. INFO.: | | | US 2003-458963P | P 20030401 |
| REFERENCE COUNT: | 7 | THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT | | |

L22 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:103660 CAPLUS
DOCUMENT NUMBER: 139:94939
TITLE: Effect of 4-hydroxytamoxifen isomers on growth and ultrastructural aspects of normal human breast epithelial (HBE) cells in culture
AUTHOR(S): Malet, Catherine; Spritzer, Poli; Cumins, Caroline; Guillaumin, Delhy; Mauvais-Jarvis, Pierre; Kutte, Frederique
CORPORATE SOURCE: Department of Endocrinology and Reproductive Medicine, Hopital Necker, Paris, 75743, Fr.
SOURCE: Journal of Steroid Biochemistry and Molecular Biology (2003), Volume Date 2002, 82(4-5), 289-296
CODEN: JSBEBZ; ISSN: 0960-0760
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L22 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:935564 CAPLUS
DOCUMENT NUMBER: 124:44960
TITLE: Phase I study of percutaneous 4-hydroxy-tamoxifen with analyses of 4-hydroxy-tamoxifen concentrations in breast cancer and normal breast tissue
AUTHOR(S): Pujol, Henri; Girault, Jacques; Rouanet, Philippe; Fournier, Sabine; Grenier, Jean; Simony, Joelle; Fourtillan, Jean-Bernard; Pujol, Jean-Louis
CORPORATE SOURCE: Cancer Institute, Montpellier University, Montpellier, F-34298, Fr.
SOURCE: Cancer Chemotherapy and Pharmacology (1995), 36(6), 493-8
CODEN: CCPHDZ; ISSN: 0344-5704
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
 ACCESSION NUMBER: 1985:620824 CAPLUS
 DOCUMENT NUMBER: 103:220824
 TITLE: Antiestrogen drug for percutaneous administration
 INVENTOR(S): Mauvais Jarvis, Pierre; Kuttenn, Frederique
 PATENT ASSIGNEE(S):
 SOURCE: PCT Int. Appl., 15 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------------|-----------------|----------|
| WO 8503228 | A1 | 19850801 | WO 1984-EP436 | 19841221 |
| W: DK, JP, US | | | | |
| RW: AT, BE, CH, DE, FR, GB, LU, NL, SE | | | | |
| FR 2558373 | A1 | 19850726 | FR 1984-927 | 19840120 |
| FR 2558373 | B1 | 19870703 | | |
| EP 151326 | A1 | 19850814 | EP 1984-201920 | 19841219 |
| EP 151326 | B1 | 19890712 | | |
| R: IT | | | | |
| EP 169214 | A1 | 19860129 | EP 1985-900469 | 19841221 |
| EP 169214 | B1 | 19920311 | | |
| R: AT, BE, CH, DE, FR, GB, LI, LU, NL, SE | | | | |
| JP 61500914 | T2 | 19860508 | JP 1985-500495 | 19841221 |
| JP 06067826 | B4 | 19940831 | | |
| AT 73334 | E | 19920315 | AT 1985-900469 | 19841221 |
| US 4919937 | A | 19900424 | US 1985-777786 | 19850913 |
| DK 8504203 | A | 19850917 | DK 1985-4203 | 19850917 |
| DK 155143 | B | 19890220 | | |
| DK 155143 | C | 19890703 | | |
| PRIORITY APPLN. INFO.: | | | | |
| | | FR 1984-927 | A 19840120 | |
| | | EP 1985-900469 | A 19841221 | |
| | | WO 1984-EP436 | W 19841221 | |

=> d kwic 4

L22 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
 TI Antiestrogen drug for percutaneous administration
 AB The title drug is a hydroalc. gel containing hydroxytamoxifen [$1-(p\text{-dimethylaminoethoxyphenyl})\text{-trans-}1-(p\text{-hydroxyphenethylbut-1-ene)}(I)$] [68047-06-3] and progesterone [57-83-0]. I is used for the treatment of breast affections, particularly benign cancerous affections. Thus, a gel is given, containing progesterone 1.5, I 0.15, Carbopol 934 1, triethanolamine 1.5 g, EtOH 50 mL, . . .
 ST topical antiestrogen pharmaceutical breast cancer
 IT Neoplasm inhibitors
 (antiestrogen pharmaceuticals, for percutaneous administration)
 IT Estrogens
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors, pharmaceuticals, for percutaneous administration)
 IT Mammary gland
 (neoplasm, treatment of, topical antiestrogen pharmaceuticals for)
 IT 68047-06-3
 RL: BIOL (Biological study)

(antiestrogen pharmaceuticals containing, for percutaneous administration)
IT 57-83-0, biological studies
RL: BIOL (Biological study)
(pharmaceuticals containing hydroxytamoxifen and, for percutaneous administration)

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 28.29 | 42.78 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -0.73 | -0.73 |

FILE 'PCTFULL' ENTERED AT 16:35:38 ON 10 AUG 2005
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FILE LAST UPDATED: 9 AUG 2005 <20050809/UP>
MOST RECENT UPDATE WEEK: 200531 <200531/EW>
FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s hydroxytamoxifen
L23 268 HYDROXYTAMOXIFEN

=> s cancer? or tumor? or neoplas?
70495 CANCER?
59135 TUMOR?
20255 NEOPLAS?
L24 88096 CANCER? OR TUMOR? OR NEOPLAS?

=> s breast or mammar?
28618 BREAST
1130 BREASTS
28849 BREAST
(BREAST OR BREASTS)
13019 MAMMAR?
L25 34444 BREAST OR MAMMAR?

=> s l24 (S) 125
L26 26782 L24 (S) L25

=> s dens?
L27 209738 DENS?

=> s l27 and l26
L28 15333 L27 AND L26

=> s l28 and l23
L29 118 L28 AND L23

=> s l29 and dense
29710 DENSE
825 DENSES
30063 DENSE
(DENSE OR DENSES)
L30 18 L29 AND DENSE

=> s l29 and density
 165069 DENSITY
 29501 DENSITIES
 170122 DENSITY
 (DENSITY OR DENSITIES)
 L31 111 L29 AND DENSITY

=> s l25 (S) densit?
 179779 DENSIT?
 L32 1644 L25 (S) DENSIT?

=> s l32 and l23
 L33 22 L32 AND L23

=> s l33 not py>2001
 398484 PY>2001
 L34 10 L33 NOT PY>2001

=> d ibib 1-5

L34 ANSWER 1 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 2001074377 PCTFULL ED 20020822
 TITLE (ENGLISH): NON-MAMMALIAN GNRH ANALOGS AND USES THEREOF IN TUMOR
 CELL GROWTH REGULATION AND CANCER THERAPY
 TITLE (FRENCH): ANALOGUES DE GNRH NON MAMMIFERE ET LEURS UTILISATIONS
 POUR LA REGULATION DE LA CROISSANCE DE CELLULES
 TUMORALES ET POUR LE TRAITEMENT DES CANCERS
 INVENTOR(S): SILER-KHODR, Theresa, M.;
 KHODR, Gabriel, S.
 PATENT ASSIGNEE(S): SILER-KHODR, Theresa, M.;
 KHODR, Gabriel, S.
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2001074377 | A1 | 20011011 |

 DESIGNATED STATES
 W:
 AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
 MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
 TR TT TZ UA UG UZ VN YA ZA ZW GH GM KE LS MW MZ SD SL
 SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
 DK ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI
 CM GA GN GW ML NE SN TD TG
 WO 2000-US26575 A 20000926
 PRIORITY INFO.: US 2000-09/540,685 20000331

L34 ANSWER 2 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 2001063292 PCTFULL ED 20020822
 TITLE (ENGLISH): COMPOSITIONS AND METHODS OF USE OF HET, A NOVEL
 MODULATOR OF ESTROGEN ACTION
 TITLE (FRENCH): COMPOSITIONS ET UTILISATIONS DE HET, UN NOUVEAU
 MODULATEUR DE L'ACTION OESTROGENIQUE
 INVENTOR(S): OESTERREICH, Steffi;
 OSBORNE, C., Kent;
 LEE, Adrian, V.;
 FUQUA, Suzanne, A.W.
 PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM;
 OESTERREICH, Steffi;
 OSBORNE, C., Kent;
 LEE, Adrian, V.;

DOCUMENT TYPE:
PATENT INFORMATION:

FUQUA, Suzanne, A.W.
Patent

NUMBER KIND DATE

WO 2001063292 A2 20010830

DESIGNATED STATES
W:

AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:
PRIORITY INFO.:

WO 2001-US6135 A 20010222
US 2000-60/184,097 20000222

L34 ANSWER 3 OF 10

PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER:
TITLE (ENGLISH):

2001000245 PCTFULL ED 20020828
HUMANIZED ANTI-ErbB2 ANTIBODIES AND TREATMENT WITH

TITLE (FRENCH):

ANTI-CORPS ANTI-ERBB2 HUMANISES ET TRAITEMENT A L'AIDE
DE CES ANTICORPS

INVENTOR(S):

ADAMS, Camellia, W.;
PRESTA, Leonard, G.;
SLIWOWSKY, Mark

PATENT ASSIGNEE(S):
DOCUMENT TYPE:
PATENT INFORMATION:

GENENTECH, INC.
Patent

NUMBER KIND DATE

WO 2001000245 A2 20010104

DESIGNATED STATES
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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL
SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF CG CI
CN GA GN GW ML MR NE SN TD TG

APPLICATION INFO.:
PRIORITY INFO.:

WO 2000-US17366 A 20000623
US 1999-60/141,316 19990625

L34 ANSWER 4 OF 10

PCTFULL COPYRIGHT 2005 Univentio on STN

ACCESSION NUMBER:
TITLE (ENGLISH):

2001000244 PCTFULL ED 20020828
METHODS OF TREATMENT USING ANTI-ErbB

TITLE (FRENCH):

METHODS DE TRAITEMENT UTILISANT DES CONJUGATES
MAYTANSINOÏDES-ANTICORPS ANTI-ERBB

INVENTOR(S):

ERICKSON, Sharon;
SCHWALL, Ralph
GENENTECH, INC.;
ERICKSON, Sharon;
SCHWALL, Ralph

PATENT ASSIGNEE(S):
DOCUMENT TYPE:
PATENT INFORMATION:

Patent

NUMBER KIND DATE

WO 2001000244 A2 20010104

DESIGNATED STATES

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
 CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
 IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
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 TR TT TZ UA UG US VN YU ZA ZW GH GM KE LS MW MZ SD
 SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
 DE DE ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG
 CI CM GA GN GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2000-US17229 A 20000623
 PRIORITY INFO.: US 1999-60/141,316 19990625
 US 2000-60/189,844 20000316

L34 ANSWER 5 OF 10 PCTFULL COPYRIGHT 2005 Univentio on STN
 ACCESSION NUMBER: 2001000238 PCTFULL ED 20020828
 TITLE (ENGLISH): TREATING PROSTATE CANCER WITH ANTI-ErbB2 ANTIBODIES
 TITLE (FRENCH): TRAITEMENT DU CANCER DE LA PROSTATE A L'AIDE DES
 ANTICORPS ANTI-ERBB2
 INVENTOR(S): AGUS, David, B.;
 SCHER, Howard, I.;
 SLIWOWSKI, Mark, X.
 GENENTECH, INC.;
 PATENT ASSIGNEE(S): SLOAN-KETTERING INSTITUTE FOR CANCER RESEARCH
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|--------------------|--|------|----------|
| DESIGNATED STATES | WO 2001000238 | A1 | 20010104 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG UZ VN YU ZA ZW GH GM KE LS MW MZ SD SL
SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY DE
DE ES FI FR GB GR IE IT LU MC NL PT SE BF BJ CF CG CI
CM GA GN GW ML MR NE SN TD TG | | |
| APPLICATION INFO.: | WO 2000-US17423 A 20000623 | | |
| PRIORITY INFO.: | US 1999-60/141,316 19990625 | | |

=> d his

(FILE 'HOME' ENTERED AT 16:27:28 ON 10 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005
 E "4-HYDROXYTAMOXIFEN"/CN 25

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005
 L2 0 S L1
 L3 666 S 4-HYDROXYTAMOXIFEN/CN
 L4 233739 S BREAST OR MAMMAR?
 L5 256821 S DENSITY
 L6 1500 S L5 (S) L4
 L7 2 S L6 AND L3

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005
 S 4-HYDROXYTAMOXIFEN/CN

FILE 'REGISTRY' ENTERED AT 16:30:42 ON 10 AUG 2005
 L8 1 S 4-HYDROXYTAMOXIFEN/CN

FILE 'CAPLUS' ENTERED AT 16:30:43 ON 10 AUG 2005

L9 1273 S L8
L10 101462 S BREAST OR MAMMAR?
L11 358546 S DENSITY
L12 235 S L10 (S) L11
L13 1 S L12 AND L9
L14 496119 S DENS?
L15 949 S L14 AND L10
L16 3 S L15 AND L9
L17 659727 S CANCER? OR TUMOR? OR NEOPLAS?
L18 73400 S L17 AND L10
L19 73400 S L18 (S) L10
L20 69226 S L17 (S) L10
L21 493 S L20 AND L8
L22 4 S L21 AND PERCUTAN?

FILE 'PCTFULL' ENTERED AT 16:35:38 ON 10 AUG 2005

L23 268 S HYDROXYTAMOXIFEN
L24 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L25 34444 S BREAST OR MAMMAR?
L26 26782 S L24 (S) L25
L27 209738 S DENS?
L28 15333 S L27 AND L26
L29 118 S L28 AND L23
L30 18 S L29 AND DENSE
L31 111 S L29 AND DENSITY
L32 1644 S L25 (S) DENSIT?
L33 22 S L32 AND L23
L34 10 S L33 NOT PY>2001

=> s percutan?
L35 11391 PERCUTAN?

=> s 135 and 123
L36 17 L35 AND L23

=> s 136 and 126
L37 16 L36 AND L26

=> s 137 and densit?
L38 179779 DENSIT?
 11 L37 AND DENSIT?

=> s 123/ab
L39 1 (HYDROXYTAMOXIFEN/AB)

=> d ibib

L39 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 1992004310 PCTFULL ED 20020513
TITLE (ENGLISH): TRIARYLETHYLENE CARBOXYLIC ACIDS WITH ESTROGENIC
 ACTIVITY
TITLE (FRENCH): ACIDES CARBOXYLIQUES DE TRIARYLETHYLENE A ACTIVITE
 ESTROGENE
INVENTOR(S): PETER, C., Ruenitz
PATENT ASSIGNEE(S): UNIVERSITY OF GEORGIA RESEARCH FOUNDATION, INC.
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|------------|------|----------|
| WO 9204310 | A1 | 19920319 |

DESIGNATED STATES

W: AT AU BE CA CH DE DK ES FR GB GR IT JP LU NL SE
APPLICATION INFO.: WO 1991-US6266 A 19910830
PRIORITY INFO.: US 1990-579,398 19900907

=> d kwic

L39 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN
ABEN . . . the RCOOH and X moieties are either
meta or para to the phenyl ethylene linkage. Examples of active
compounds include 4-hydroxytamoxifen
acid, 3-hydroxytamoxifen acid, 4-[1-(p-hydroxyphenyl)-2-phenyl-
1-buten-yl]benzoic acid and
4-[1-(p-hydroxyphenyl)-2-phenyl-1-buten-yl]phenylacetic acid.
Compositions containing these
triarylethylene carboxylic acids can be administered to patients to
alleviate medical. . .
ABFR . . . meta soit para
par rapport a la liaison ethylene phenylique. On peut citer a titre
d'exemples de composes actifs
l'acide 4-hydroxytamoxifen, l'acide 3-hydroxytamoxifen
, l'acide
4-[1-(p-hydroxyphenyle)-2-phenyle-1-butene-yl]benzoique et l'acide
4-[1-(p-hydroxyphenyle)-2-phenyle-1-butene-yl]phenylacetique. On peut
administrer des compositions
contenant ces acides carboxyliques de triarylethylene a des patients
afin. . .

=> d his

(FILE 'HOME' ENTERED AT 16:27:28 ON 10 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005
E "4-HYDROXYTAMOXIFEN"/CN 25

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005

L2 0 S L1
L3 666 S 4-HYDROXYTAMOXIFEN/CN
L4 233739 S BREAST OR MAMMAR?
L5 256821 S DENSITY
L6 1500 S L5 (S) L4
L7 2 S L6 AND L3

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005
S 4-HYDROXYTAMOXIFEN/CN

FILE 'REGISTRY' ENTERED AT 16:30:42 ON 10 AUG 2005
L8 1 S 4-HYDROXYTAMOXIFEN/CN

FILE 'CAPLUS' ENTERED AT 16:30:43 ON 10 AUG 2005
L9 1273 S L8
L10 101462 S BREAST OR MAMMAR?
L11 358546 S DENSITY
L12 235 S L10 (S) L11
L13 1 S L12 AND L9
L14 496119 S DENS?
L15 949 S L14 AND L10
L16 3 S L15 AND L9
L17 659727 S CANCER? OR TUMOR? OR NEOPLAS?

L18 73400 S L17 AND L10
L19 73400 S L18 (S) L10
L20 69226 S L17 (S) L10
L21 493 S L20 AND L8
L22 4 S L21 AND PERCUTAN?

FILE 'PCTFULL' ENTERED AT 16:35:38 ON 10 AUG 2005

L23 268 S HYDROXYTAMOXIFEN
L24 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L25 34444 S BREAST OR MAMMAR?
L26 26782 S L24 (S) L25
L27 209738 S DENSIT?
L28 15333 S L27 AND L26
L29 118 S L28 AND L23
L30 18 S L29 AND DENSE
L31 111 S L29 AND DENSITY
L32 1644 S L25 (S) DENSIT?
L33 22 S L32 AND L23
L34 10 S L33 NOT PY>2001
L35 11391 S PERCUTAN?
L36 17 S L35 AND L23
L37 16 S L36 AND L26
L38 11 S L37 AND DENSIT?
L39 1 S L23/AB

=> s tamoxifen
5058 TAMOXIFEN
15 TAMOXIFENS
L40 5061 TAMOXIFEN
(TAMOXIFEN OR TAMOXIFENS)

=> s l40/ti
L41 25 (TAMOXIFEN/TI)

=> s l40/ab
67 TAMOXIFEN/AB
2 TAMOXIFENS/AB
L42 67 (TAMOXIFEN/AB)
(TAMOXIFEN OR TAMOXIFENS)/AB)

=> s l42 or l47
L47 NOT FOUND
The L-number entered could not be found. To see the definition
of L-numbers, enter DISPLAY HISTORY at an arrow prompt (>).

=> s l42 or l41
L43 70 L42 OR L41

=> s l43 and 126
L44 58 L43 AND L26

=> s l44 and percutan?
11391 PERCUTAN?
L45 6 L44 AND PERCUTAN?

=> s l45 and densit?
179779 DENSIT?
L46 6 L45 AND DENSIT?

=> s densit? (S) 125
179779 DENSIT?
L47 1644 DENSIT? (S) L25

=> s 147 and 146
L48 2 L47 AND L46

=> d ibib 1-2

L48 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2004087123 PCTFULL ED 20041019 EW 200442
TITLE (ENGLISH): PREVENTION AND TREATMENT OF BREAST
CANCER WITH 4-HYDROXY TAMOXIFEN
TITLE (FRENCH): PREVENTION ET TRAITEMENT DU CANCER DU SEIN A L'AIDE DE
4-HYDROXY TAMOXIFENE
INVENTOR(S): SALIN-DROUIN, Dominique, 32, rue des Gatines, F-91370
Verrieres-le-Buisson, FR;
WEPIERRE, Jacques, 1, rue Valoise, F-77166 Grisy
Suisnes, FR;
ROUANET, Philippe, 154, rue des Quatre Seigneurs,
F-34090 Montpellier, FR
PATENT ASSIGNEE(S): LABORATOIRES BESINS INTERNATIONAL, 5, rue du Bourg
l'Abbe, F-75003 Paris, FR [FR, FR]
AGENT: NARGOLWALLA, Cyra\$, Cabinet Plasseraud, 65/67, rue de
la Victoire, F-75440 Paris Cedex 09\$, FR
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|--------|------|------|
|--------|------|------|

WO 2004087123 A1 20041014

DESIGNATED STATES
W:
AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
MG MM MN MW MX MZ NI NO NZ OM PG PH PL PT RO RU SC SD
SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA
ZM ZW
BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
AM AZ BY KG KZ MD RU TJ TM
AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
MC NL PT RO SE SI SK TR
BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
RW (ARIGO): WO 2003-EP15029 A 20031215
RW (EAPO):
RW (EPO):
RW (OAPI):
APPLICATION INFO.: US 2003-60/458,963 20030401
PRIORITY INFO.:

L48 ANSWER 2 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2004054558 PCTFULL ED 20040707 EW 200427
TITLE (ENGLISH): REDUCTION OF BREAST DENSITY WITH
4-HYDROXY TAMOXIFEN
TITLE (FRENCH): REDUCTION DE LA DENSITE MAMMAIRE A L'AIDE DE
4-HYDROXY TAMOXIFENE
INVENTOR(S): BUA, Jay, 3100 Saddle Crest Lane, Oakton, VA 22124, US
PATENT ASSIGNEE(S): LABORATOIRES BESINS INTERNATIONAL, 5, rue du Bourg
l'Abbe, F-75003 Paris, FR [FR, FR]
AGENT: NARGOLWALLA, Cyra\$, Cabinet Plasseraud, 65/67, rue de
la Victoire, F-75440 Paris Cedex 9\$, FR
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
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WO 2004054558 A2 20040701

DESIGNATED STATES

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 SE SG SK SL SY TJ TM TN TR TT TZ UA UG UZ VC VN YU ZA
 ZM ZW

RW (ARIPO): BW GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW

RW (EAPO): AN AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IT LU
 MC NL PT RO SE SI SK TR

RW (OAPI): BE BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2003-EP15030 A 20031215

PRIORITY INFO.: US 2002-60/433,958 20021218

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(FILE 'HOME' ENTERED AT 16:27:28 ON 10 AUG 2005)

FILE 'REGISTRY' ENTERED AT 16:27:48 ON 10 AUG 2005
 E "4-HYDROXYTAMOXIFEN"/CN 25

L1 1 S E3

FILE 'MEDLINE' ENTERED AT 16:28:48 ON 10 AUG 2005

| | |
|----|-----------------------------|
| L2 | 0 S L1 |
| L3 | 666 S 4-HYDROXYTAMOXIFEN/CN |
| L4 | 233739 S BREAST OR MAMMAR? |
| L5 | 256821 S DENSITY |
| L6 | 1500 S L5 (S) L4 |
| L7 | 2 S L6 AND L3 |

FILE 'CAPLUS' ENTERED AT 16:30:37 ON 10 AUG 2005
 S 4-HYDROXYTAMOXIFEN/CNFILE 'REGISTRY' ENTERED AT 16:30:42 ON 10 AUG 2005
 L8 1 S 4-HYDROXYTAMOXIFEN/CN

FILE 'CAPLUS' ENTERED AT 16:30:43 ON 10 AUG 2005

| | |
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| L9 | 1273 S L8 |
| L10 | 101462 S BREAST OR MAMMAR? |
| L11 | 358546 S DENSITY |
| L12 | 235 S L10 (S) L11 |
| L13 | 1 S L12 AND L9 |
| L14 | 496119 S DENS? |
| L15 | 949 S L14 AND L10 |
| L16 | 3 S L15 AND L9 |
| L17 | 659727 S CANCER? OR TUMOR? OR NEOPLAS? |
| L18 | 73400 S L17 AND L10 |
| L19 | 73400 S L18 (S) L10 |
| L20 | 69226 S L17 (S) L10 |
| L21 | 493 S L20 AND L8 |
| L22 | 4 S L21 AND PERCUTAN? |

FILE 'PCTFULL' ENTERED AT 16:35:38 ON 10 AUG 2005

| | |
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| L23 | 266 S HYDROXYTAMOXIFEN |
| L24 | 88096 S CANCER? OR TUMOR? OR NEOPLAS? |
| L25 | 34444 S BREAST OR MAMMAR? |
| L26 | 26782 S L24 (S) L25 |
| L27 | 209738 S DENS? |
| L28 | 15333 S L27 AND L26 |
| L29 | 118 S L28 AND L23 |

| | | |
|-----|-------|---------------------|
| L30 | 18 | S L29 AND DENSE |
| L31 | 111 | S L29 AND DENSITY? |
| L32 | 1644 | S L25 (S) DENSIT? |
| L33 | 22 | S L32 AND L23 |
| L34 | 10 | S L33 NOT PY>2001 |
| L35 | 11391 | S PERCUTAN? |
| L36 | 17 | S L35 AND L23 |
| L37 | 16 | S L36 AND L26 |
| L38 | 11 | S L37 AND DENSIT? |
| L39 | 1 | S L23/AB |
| L40 | 5061 | S TAMOXIFEN |
| L41 | 25 | S L40/TI |
| L42 | 67 | S L40/AB |
| L43 | 70 | S L42 OR L41 |
| L44 | 58 | S L43 AND L26 |
| L45 | 6 | S L44 AND PERCUTAN? |
| L46 | 6 | S L45 AND DENSIT? |
| L47 | 1644 | S DENSIT? (S) L25 |
| L48 | 2 | S L47 AND L46 |

⇒

---Logging off of STN---

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Executing the logoff script...

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| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| FULL ESTIMATED COST | ENTRY | SESSION |
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| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| CA SUBSCRIBER PRICE | ENTRY | SESSION |
| | 0.00 | -0.73 |

STN INTERNATIONAL LOGOFF AT 16:42:33 ON 10 AUG 2005

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID: SSSPTA1642BJF

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 28 PATDPAFULL - New display fields provide for legal status

NEWS 4 FEB 28 data from INPADOC
NEWS 5 MAR 02 BABS - Current-awareness alerts (SDIs) available
NEWS 6 MAR 03 GBFULL: New full-text patent database on STN
NEWS 7 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS 8 MAR 22 MEDLINE file segment of TOXCENTER reloaded
NEWS 9 MAR 22 KOREPAT now updated monthly; patent information enhanced
NEWS 10 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS 11 MAR 22 PATDASPAC - New patent database available
NEWS 12 APR 04 REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS 13 APR 04 EPFULL enhanced with additional patent information and new fields
NEWS 14 APR 18 EMBASE - Database reloaded and enhanced
NEWS 15 APR 25 New CAS Information Use Policies available online
NEWS 16 APR 28 Patent searching, including current-awareness alerts (SDIs),
based on application date in CA/Cplus and USPATFULL/USPAT2
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FILE COVERS 1978 TO DATE

>>> IMAGES ARE AVAILABLE ONLINE AND FOR EMAIL-PRINTS <<<

=> s hydroxytamoxifen or (hyrdroxy tamoxifen)

268 HYDROXYTAMOXIFEN
13 HYDRDROXY
5058 TAMOXIFEN
15 TAMOXIFENS
5061 TAMOXIFEN
(TAMOXIFEN OR TAMOXIFENS)
0 HYDRDROXY TAMOXIFEN
(HYDRDROXY (W) TAMOXIFEN)

L1 268 HYDROXYTAMOXIFEN OR (HYDRDROXY TAMOXIFEN)

=> s tamoxifen

5058 TAMOXIFEN
15 TAMOXIFENS
5061 TAMOXIFEN
(TAMOXIFEN OR TAMOXIFENS)

=> s 12/ab

67 TAMOXIFEN/AB
2 TAMOXIFENS/AB
L3 67 (TAMOXIFEN/AB)
(TAMOXIFEN OR TAMOXIFENS)/AB)

=> s 12/ti

L4 25 (TAMOXIFEN/TI)

=> s 14 or 12

L5 5061 L4 OR L2

=> s 14 or 13

L6 70 L4 OR L3

=> s breast or mammar

=> s breast or mammar?
28618 BREAST
1130 BREASTS
28849 BREAST
(BREAST OR BREASTS)
13019 MAMMAR?

L7 34444 BREAST OR MAMMAR?

=> s cancer? or tumor? or neoplas?

70495 CANCER?
59135 TUMOR?
20255 NEOPLAS?
L8 88096 CANCER? OR TUMOR? OR NEOPLAS?

=> s 17/ab

1789 BREAST/AB
86 BREASTS/AB
1818 BREAST/AB
(BREAST OR BREASTS)/AB)
241 MAMMAR?/AB

L9 2015 (BREAST/AB OR MAMMAR?/AB)

=> s 19 and 18
L10 1529 L9 AND L8

=> s percutaneous? or topical?
10644 PERCUTANEOUS?
49656 TOPICAL?
L11 57173 PERCUTANEOUS? OR TOPICAL?

=> s l11 and l10
L12 498 L11 AND L10

=> d his

(FILE 'HOME' ENTERED AT 08:51:47 ON 11 AUG 2005)

FILE 'PCTFULL' ENTERED AT 08:52:01 ON 11 AUG 2005
L1 268 S HYDROXYTAMOXIFEN OR (HYDRDROXY TAMOXIFEN)
L2 5061 S TAMOXIFEN
L3 67 S L2/AB
L4 25 S L2/TI
L5 5061 S L4 OR L2
L6 70 S L4 OR L3
L7 34444 S BREAST OR MAMMAR?
L8 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L9 2015 S L7/AB
L10 1529 S L9 AND L8
L11 57173 S PERCUTANEOUS? OR TOPICAL?
L12 498 S L11 AND L10

=> s l12 and 16
L13 10 L12 AND L6

=> s l13 and 11
L14 5 L13 AND L1

=> s l14 not py>2002
294498 PY>2002
L15 1 L14 NOT PY>2002

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L15 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2001063292 PCTFULL ED 20020822
TITLE (ENGLISH): COMPOSITIONS AND METHODS OF USE OF HET, A NOVEL
MODULATOR OF ESTROGEN ACTION
TITLE (FRENCH): COMPOSITIONS ET UTILISATIONS DE HET, UN NOUVEAU
MODULATEUR DE L'ACTION OESTROGENIQUE
INVENTOR(S): OESTERREICH, Steffi;
OSBORNE, C., Kent;
LEE, Adrian, V.;
FUQUA, Suzanne, A.W.
PATENT ASSIGNEE(S): BOARD OF REGENTS, THE UNIVERSITY OF TEXAS SYSTEM;
OESTERREICH, Steffi;
OSBORNE, C., Kent;
LEE, Adrian, V.;
FUQUA, Suzanne, A.W.
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|--------|------|------|
|--------|------|------|

DESIGNATED STATES

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A2 20010830

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AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
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DE DE ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
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APPLICATION INFO.:

WO 2001-US6135 A 20010222

PRIORITY INFO.:

US 2000-60/184,097 20000222

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L15 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN
ABEN Estrogen Receptor; Nuclear Matrix Protein HET/SAF-B; Transcription;
Repression; Antiestrogen; Tamoxifen. Disclosed are methods for
the detection of tumor cells, in particular human
breast cancer cells. Genetic and antibody probes and
methods useful in determining the presence of and monitoring
tumor cell proliferation are also described. The methods involve
determining HET polypeptide expression, mRNA levels or loss of
heterozygosity at human chromosomal locus 19p13 as a measure of
tumor cell malignancy. These methods are also of use in
distinguishing breast cancers that are resistant to
estrogen antagonists, such as tamoxifen, from estrogen
antagonist sensitive tumors. Also described are procedures for
transforming cells with HET gene containing vectors that express HET
polypeptide. Such procedures may be of use in converting
tamoxifen-resistant tumors into tamoxifen
-sensitive tumors.

ABFR Mots-clés : receiteur d'oestrogene ; protéine de matrice nucléaire
HET/SAF-B ; transcription, répression; anti-oestrogene; tamoxifène
L'invention concerne des procédés de détection de cellules
tumoriales, en particulier de cellules du cancer du
sein humain. Elle concerne en outre des sondes génétiques et des sondes
d'anticorps ainsi que des procédés servant à déterminer la présence
d'une prolifération de cellules tumorales et des surveiller
celle-ci. Ces procédés consistent à mesurer l'expression du polypeptide
HET, les taux d'ARNm ou la perte du caractère hétérozygote dans le locus
chromosomique 19p13, afin de déterminer le degré de malignité des
cellules tumorales. Ces procédés permettent en outre de
distinguer les cancers du sein résistants aux antagonistes de
l'oestrogene tels que le tamoxifène, des tumeurs sensibles aux
antagonistes de l'oestrogene. L'invention concerne en outre des
procédures consistant à transformer des cellules avec des vecteurs
contenant un gène HET exprimant le polypeptide HET. Ces procédures
peuvent être utiles pour convertir les tumeurs résistantes au tamoxifène
en tumeurs sensibles au tamoxifène.

=> d kwic

L15 ANSWER 1 OF 1 PCTFULL COPYRIGHT 2005 Univentio on STN
ABEN Estrogen Receptor; Nuclear Matrix Protein HET/SAF-B; Transcription;
Repression; Antiestrogen; Tamoxifen. Disclosed are methods for
the detection of tumor cells, in particular human
breast cancer cells. Genetic and antibody probes and
methods useful in determining the presence of and monitoring
tumor cell proliferation are also described. The methods involve

determining HET polypeptide expression, mRNA levels or loss of heterozygosity at human chromosomal locus 19p13 as a measure of tumor cell malignancy. These methods are also of use in distinguishing breast cancers that are resistant to estrogen antagonists, such as tamoxifen, from estrogen antagonist sensitive tumors. Also described are procedures for transforming cells with HET gene containing vectors that express HET polypeptide. Such procedures may be of use in converting tamoxifen-resistant tumors into tamoxifen -sensitive tumors.

ABFR . . . d'oestrogene ; proteine de matrice nucleaire HET/SAF-B ; transcription, repression; anti-oestrogene; tamoxifene L'invention concerne des procedes de detection de cellules tumorales, en particulier de cellules du cancer du sein humain. Elle concerne en outre des sondes genetiques et des sondes d'anticorps ainsi que des procedes servant a determiner la presence d'une proliferation de cellules tumorales et des surveiller celle-ci. Ces procedes consistent a mesurer l'expression du polypeptide HET, les taux d'ARNm ou la perte du caractere heterozygote dans le locus chromosomique 19p13, afin de determiner le degre de malignite des cellules tumorales . Ces procedes permettent en outre de distinguer les cancers du sein resitants aux antagonistes de l'oestrogene tels que le tamoxifene, des tumeurs sensibles aux antagonistes de l'oestrogene. L'invention concerne. . .

DETD 1.1 Field of the Invention
The present invention relates generally to cancer biology. In particular, it concerns novel methods and compositions for modulating estrogen actions. The present invention further relates to detection, diagnosis and prognosis of breast cancer and the identification of tamoxifen-resistant breast cancers. Another aspect of the present invention relates to gene therapy for altering the phenotype of tumor cells.

More particularly, it concerns use of expression vectors comprising an HET gene to increase the sensitivity of the tumor cell to estrogen antagonists, or to decrease the sensitivity of the tumor cell to estrogen and estrogen agonists.

Hsp27 plays a role in both growth and drug resistance of human breast cancer cells in culture (Oesterreich et al., 1993). Hsp27 has been found to contribute to increased drug resistance in CHO cells (Lavoie et al., 1993), colon cancer cells (Garrido et al., 1996), and testis cancer cells (Richards et al., 1996). Elevated hsp27 levels also correlate with increased invasion of human breast cancer cells (Lemieux et al., 1996). Hsp 27 is not an independent prognostic marker for breast cancer (Oesterreich et al., 1996b). However, hsp27 predicts a significantly worse outcome in 10, a subset of ER-positive/untreated breast cancer patients (Oesterreich et al., 1996b).

Expression of hsp27 is strongly correlated with the expression of ER in

breast tumors
. (Oesterreich et al., 1996b). Several groups have tried to decrease the expression of heat shock proteins in order to circumvent drug resistance in tumors. For example, the antiestrogen tamoxifene (Mahvi et al., 1996) and the bioflavonoid quercetin (Sliutz et 15 aL, 1996) both decrease hsp. . .

Current therapies for breast cancer are targeted, at least in part, to the estrogen receptor. A group of compounds known as selective estrogen receptor modulators (SERMs) may be used in the prevention and treatment of breast cancer (Minton, 1999). These compounds mediate agonist or antagonist effects of estrogen on the ER.

However, certain breast cancers are antiestrogen resistant, and it is not unusual, for resistance to develop following antiestrogen therapy. A need exists in the art to distinguish those tumors that are sensitive to antiestrogens from those that are resistant. A method of converting antiestrogen-resistant tumors to antiestrogen-sensitive tumors would be of great benefit for treatment of breast cancer.

. THE INVENTION

The present invention resolves a need in the art for a diagnostic method to differentiate between antiestrogen-resistant and antiestrogen-sensitive breast tumors.

Also provided are compositions and methods of use in converting antiestrogen-resistant to antiestrogen-sensitive tumors, by administering expression vectors comprising an BET coding sequence. Specific examples include compositions and methods of use in differentiating antiestrogen-resistant and antiestrogen-sensitive tumors and in converting antiestrogen-resistant to antiestrogen-sensitive tumors.

Specific antiestrogens that are within the context of the invention include the nonsteroidal compounds Tamoxifen, Toremifene, Idoxifene, Droloxfene, TAT-59, Zindoxfene, Trioxifene, and. . . the steroid antiestrogens ICI 182,780 (FASLODEX™) and EM Tamoxifen is a particularly well-known estrogen antagonist that exhibits efficacy for treatment of breast cancer. Some of the other nonsteroidal compounds, e.g. TAT-59, are metabolized into an active metabolite of Tamoxifen or are analogues of Tamoxifen, e.g.. . .

. linked to the region encoding said protein, under conditions effective for the uptake and expression of said nucleic acid by said tumor cell, wherein said cell is

converted from a phenotype displaying normal steroid hormone receptor activity to one displaying reduced steroid hormone receptor. . .

Of course, as detailed herein, some of the primary embodiments of the present invention entail the diagnosing and treatment of breast cancer. Exemplary forms of breast cancer that may be diagnosed and/or treated according to the invention include infiltrating duct carcinoma, lobular carcinoma, medullary carcinoma, mucinous carcinoma, tubular carcinoma, . . .

In some embodiments, the invention relates to methods for detecting resistance to antiestrogens in breast cancer cells, comprising: a) obtaining a sample suspected of containing breast cancer cells; b) contacting said sample with an antibody that specifically binds to an BET polypeptide under conditions effective to bind said antibody. . .

Western blotting, ELISA, Northern blotting, slot blotting, dot blotting and/or DNA chip assay. Alternative embodiments include methods for predicting antiestrogen resistance in breast cancer cells, comprising: a) measuring the amount of BET gene product in a sample containing breast cancer cells; and b) comparing the amount of BET gene product present in said sample with the amount of BET gene product in samples selected from patients with antiestrogen-resistant and antiestrogen-sensitive breast cancers. Exemplary antiestrogens can be selected from the group consisting of Tamoxifen, Torenfene, Idoxifene, Droloxifene, TAT-59, Zindoxifene, Trioxifene, Raloxifene, ICI 182,780 and EM. . .

The invention also relates to method for predicting antiestrogen resistance in breast cancer cells, comprising: a) obtaining a breast cancer cell sample and a normal cell sample from the same individual; b) amplifying chromosomal DNA from said breast cancer and normal cell samples using primers selected to amplify a chromosomal locus comprising the BET gene; and c) comparing the amplification products from said breast cancer and normal cells, wherein loss of heterozygosity (LOH) at said locus indicated by an amplification product present in the normal cell and missing in the breast cancer cell is indicative of antiestrogen resistance in said breast cancer cell.

In a further embodiment, the invention anticipates methods for detecting anti-estrogen resistance in breast cancer cells, comprising: a)

obtaining a sample suspected of containing breast cancer cells; b) measuring the amount of BET gene product in said sample,] wherein said BET gen& product is a molecule. . . in the amount of BET gene product in said sample compared with the amount in normal cells indicates anti-estrogen resistance of breast cancer cells.

The invention further encompasses methods of malignant breast cancer diagnosis, comprising determining loss of heterozygosity (LOH) at a chromosomal locus comprising the BET gene, wherein LOH at said locus is indicative of antiestrogen resistance in breast cancer cells. Likewise, the invention encompasses methods of determining likelihood of survival for a breast tumor subject, comprising determining loss of heterozygosity (LOH) at a chromosomal locus comprising the BET gene in a breast tumor cell sample from said subject, wherein LOH at said locus is associated with a decreased probability of survival.

The invention further contemplates methods for altering the phenotype of a breast tumor cell comprising contacting the cell with a nucleic acid comprising (i) a DNA sequence encoding a BET protein and (ii) a promoter active in said breast tumor cell, wherein said promoter is operably linked to the region encoding said protein, under conditions effective for the uptake and expression of said nucleic acid by said tumor cell. In some exemplary embodiments, the BET protein has the amino acid sequence of SEQ ID NO:2. For example, the breast tumor cell may be converted from a phenotype resistant to antiestrogen to a phenotype sensitive to antiestrogen. In this case, the antiestrogen may. . .

FIG. 6A and FIG. 611. BET/SAF-B expression is decreased in antiestrogen-resistant xenograft tumors.

FIG. 7 illustrates a human metaphase spread with the BET PI probe fluorescently labeling both chromosome 19 homologs at 19p13 >p13.3 FIG. 8 shows an LOH analysis at human chromosomal locus 19p13 of breast tumor specimens. Breast biopsy DNA (normal and tumor) was analyzed using PCRTm based microsatellite markers corresponding to 19-pter (Genethon, see Gyapay et al., 1994).

FIG. 9 illustrates HET expression in primary breast cancers. Frozen tumor powder was homogenized in 5% SDS, and 25 Jig protein was resolved on 7.5% PAGE. After transferring onto nitrocellulose, BET was detected. . .

FIG. 11 shows that transient transfection of antisense BET into 293 cancer cells causes an increased rate of cell division, as measured by [³H]-thymidine incorporation into DNA. Cells were transfected with 0.02, 0.2. . . .

activity, it is meant that the molecule in question has the ability to inhibit cell transformation, or to prevent metastasis or invasive tumor growth. Other phenotypes that may be regulated by the normal BET gene product are angiogenesis, cell adhesion, migration, cell-to-cell signaling, cell growth,. . . .

The term tumor suppressor is well-known to those of skill in the art.

Examples of other tumors suppressors are p53, Rb and p16, to name a few. While these molecules are structurally distinct, they form a group of functionally-related molecules, of which BET is a member. The uses for which these other tumor suppressors now are being exploited are equally applicable here.

The inventors have discovered that the gene encoding the BET protein (the 1 5 HET gene) is a tumor suppressor gene. BET has been mapped to chromosomal locus 19p13 p13 Using LOH technology, it was found that this locus is lost in 50-60% of breast cancer patients, which is higher than the LOH described for any other tumor suppressor gene described to date (e.g., p53, Rb).

the entire BET molecule, the present invention also relates to fragments of the polypeptide that may or may not retain the tumor suppressing (or other) activity of BET. Fragments including the N-terminus of the molecule may be generated by genetic engineering of translation stop. . . .

Encoding HET
Nucleic acids according to the present invention may encode an entire BET gene, a domain of BET that expresses a tumor suppressing function, or any other fragment of the BET sequences set forth herein. The nucleic acid may be derived from genomic DNA. . . .

4 5 Antisense Constructs
In some cases, mutant tumor suppressors may not be non-functional. Rather, they may have aberrant functions that cannot be overcome by replacement gene therapy, even where the. . . .

4 6 Ribozymes
Another approach for addressing the dominant negative mutant tumor

suppressor is through the use of ribozymes. Although proteins traditionally have been used for catalysis of nucleic acids, another class of macromolecules. . .

I (TN 1)

Platelet-Derived Growth Factor

Duchenne Muscular Dystrophy

SV40

ENHA-NCER/PROMOTER

Polyoma,

Retroviruses

Papilloma, Virus

Hepatitis B Virus

Human Immunodeficiency Virus

Cytomegalovirus

TABLE3

Element Inducer

Mr II Phorbol Ester (TPA)

Heavy metals

MMTV (mouse mammary tumor Glucocorticoids virus)

P-Interferon poly(rl)X

poly(rc)

Adenovirus 5 E2 Ela

c-jun Phorbol Ester (TPA), H202

Collagenase Phorbol Ester (TPA)

Stromelysin Phorbol Ester (TPA), IOL-1

SV40 Phorbol Ester (TPA)

Murine NIX. . . Interferon, Newcastle Disease Virus

GRP78 Gene A23187

a Macroglobulin IL-6

Vitnenin Serum

MHC Class I Gene H-2kB Interferon

HSP70 Ela, SV40 Large T Antigen

Proliferin Phorbol Ester-TPA

Tumor Necrosis Factor FMA

Thyroid Stimulating Hormone a Thyroid Non-none

Gene

Insulin E Box Glucose

Where a cDNA insert is employed, typically one will typically. . .

that a

nucleic acid encoding a BET gene also may be specifically delivered into a cell type

such as lung, epithelial, or tumor cells, by any number of receptor-ligand systems with or without liposomes. For example, epidermal growth factor (EGF) may be used as

the receptor for mediated delivery of a nucleic acid encoding a gene in many tumor cells that exhibit upregulation of EGF receptor. Mannose can be used to target the

mannose receptor on liver cells. Also, antibodies to. . .

most widely used means of large scale production of cells and cell products. However, suspension cultured cells have limitations, such as tumorigenic potential and lower protein production than adherent T-cells.

of the type that was used to provide the somatic and myeloma cells for the original fusion. The injected animal develops

tumors
secreting the specific monoclonal antibody produced by the fused cell
hybrid. The
body fluids of the animal, such as serum or ascites. . . .

4.4 Diagnosing Cancers Involving HET
The present inventors have determined that alterations in BET
are associated
with breast cancer and may be associated with other
malignancies. Therefore, BET
and the corresponding gene may be employed as a diagnostic or prognostic
indicator
of cancer. More specifically, point mutations, deletions,
insertions, allelic loss, or
regulatory perturbations relating to BET may cause cancer or
promote cancer
development, cause or promote tumor progression at a primary
site, and/or cause or
promote metastasis. Other phenomena associated with malignancy that may
be
affected by BET expression. . . .

Another aspect of the present invention concerns distinguishing
tamoxifen-
sensitive from tamoxifen-resistant cancers, more particularly
breast cancers.

Tamoxifen resistance is associated with decreased levels of BET gene
products in
breast cancer cells. Determination of BET expression levels,
by assay of BET mRNA
or protein, may be used to distinguish tumors that are
resistant to estrogen antagonists
(such as tamoxifen) from tumors that are sensitive to estrogen
antagonists.

Alternatively, LOH assay may be used to identify tumors that
have lost an allele of the
BET gene. Such tumors are expected to show a decreased
expression of HET gene
product.

alterations in the expressed product in a
biological sample. In particular, the present invention relates to the
diagnosis or
prognosis of breast cancer.

a patient with a
sufficiently large reference group of normal patients and patients that
have BET-
related pathologies, such as malignant breast tumors. In this
way, it is possible to
correlate the amount or type of BET detected (for example, mutant or
truncated BET
polypeptides) with various clinical states. In particular applications,
such as breast
cancers, it is contemplated that different levels of
progression of breast cancer may be
identified. In further embodiments, the sensitivity of tumors
to estrogen antagonists,
such as tamoxifen, may be determined.

5 The amplified sequences may then be identified and quantitated. The presence of the BET gene or mutants thereof may be used in the methods disclosed herein to determine degree of malignancy, cell tumorigenicity, and potential prognosis/diagnosis of cancers such as breast cancers.

as ELISA and Western blotting. This may provide a screen for the presence or absence of malignancy, as a predictor of future cancer, or to distinguish tamoxifen-resistant from tamoxifen-sensitive tumors.

or inhibition or stimulation of cell-to-cell signaling, growth, metastasis, cell division, cell migration, soft agar colony formation, contact inhibition, invasiveness, angiogenesis, apoptosis, tumor progression or other malignant phenotype. Preferred embodiments include assay of cell replication by incorporation of radiolabeled thymidine or colony formation. A preferred. . .

the use of various animal models. By developing or isolating mutant cells lines that fail to express normal BET, one can generate cancer models in mice that will be predictive of cancers in humans and other mammals. These models may employ the orthotopic or systemic administration of tumor cells to mimic primary and/or metastatic cancers. Alternatively, one may induce cancers in animals by providing agents known to be responsible for certain events associated with malignant transformation and/or tumor progression. Finally, transgenic animals (discussed below) that lack a wild-type BET may be utilized as models for cancer development and treatment.

any route that could be utilized for clinical or non-clinical purposes, including but not limited to oral, nasal, buccal, rectal, vaginal or topical. Alternatively, administration may be by intratracheal instillation, bronchial instillation, intradermal, subcutaneous, intramuscular, intraperitoneal or intravenous injection. Specifically contemplated are systemic intravenous injection, regional. . .

a compound in vivo may involve a variety of different criteria. Such criteria include, but are not limited to, survival, reduction of tumor burden or mass, arrest or slowing of tumor progression, elimination of tumors, inhibition or prevention of metastasis, increased activity level, improvement in immune effector function and improved food intake.

The present invention also contemplates, in another embodiment, the treatment of cancer. The types of cancer that may be treated, according to the present invention, are limited only by the involvement of BET. By involvement is meant that, it is not even a requirement that BET be mutated or abnormal - the overexpression of this

tumor suppressor may actually overcome other lesions within the cell. Thus, it is contemplated that a wide variety of tumors may be treated using BET therapy.

In many contexts, it is not necessary that the tumor cell be killed or induced to undergo normal cell death or apoptosis. Rather, to accomplish a meaningful treatment, all that is required is that the tumor growth be slowed to some degree. It may be that the tumor growth is completely blocked, however, or that some tumor regression is achieved. Clinical terminology such as remission and reduction of tumor burden also are contemplated given their normal usage.

In further embodiments, the treatment of cancer with BET therapy may be directed towards malignancies that are or are likely to become resistant to therapeutic compounds. In one embodiment, BET therapy may be used to treat cancer cells that have become resistant to compounds that inhibit steroid receptors. In another embodiment, BET therapy may be used to treat cells. . .

the therapeutic embodiments contemplated by the present inventors is the intervention, at the molecular level, in the events involved in the tumorigenesis of some cancers. Specifically, the present inventors intend to provide, to a cancer cell, an expression construct capable of providing BET to that cell. Any of the gene sequence variants discussed above which would encode. . .

Various routes are contemplated for various tumor types. The section below on routes contains an extensive list of possible routes. For practically any tumor, systemic delivery is contemplated. This will prove especially important for attacking microscopic or metastatic cancer. Where discrete tumor mass may be identified, a variety of direct, local and regional approaches may be taken. For example, the tumor may be injected directly with the expression vector. A tumor bed may be treated prior to, during or after resection. Following resection, one generally will deliver the vector by a catheter left in place following surgery. One may utilize the tumor vasculature to introduce the vector into the tumor by injecting a supporting vein or artery. A more

distal blood supply route also may be utilized.

different embodiment, ex vivo gene therapy is contemplated. This approach is particularly suited, although not limited, to treatment of bone marrow associated cancers. In an ex vivo embodiment, cells from the patient are removed and maintained outside the body for at least some period of time. During this period, a therapy is delivered, after which the cells are reintroduced into the patient. Preferably, any tumor cells in the sample have been killed.

own bone marrow donor. Thus, a normally lethal dose of irradiation or chemotherapeutic may be delivered to the patient to kill tumor cells, and the bone marrow repopulated with the patient's own cells that have been maintained (and perhaps expanded) ex vivo. Because bone marrow is often contaminated with tumor cells, it is desirable to purge the bone marrow of these cells. Use of gene therapy to accomplish this goal is yet. . .

4.2 Immunotherapies

Immunotherapeutics, generally, rely on the use of immune effector cells and molecules to target and destroy cancer cells. The immune effector may be, for example, an antibody specific for some marker on the surface of a tumor cell. The antibody alone may serve as an effector of therapy or it may recruit other cells to actually effect cell killing. . . targeting agent. Alternatively, the effector may be a lymphocyte carrying a surface molecule that interacts, either directly or indirectly, with a tumor cell target. Various effector cells include cytotoxic T cells and NK cells.

part of a combined therapy, in conjunction with BET-targeted gene therapy. The general approach for combined therapy is discussed below. Generally, the tumor cell must bear some marker that is amenable to targeting, i.e., is not present on the majority of other cells. Many tumor markers exist and any of these may be suitable for targeting in the context of the present invention. Common tumor markers include carcinoembryonic antigen, prostate specific antigen, urinary tumor associated antigen, fetal antigen, tyrosinase (p97), gp68, TAG-72, MUG, sialyl Lewis antigen, MucA, MucB, PLAP, estrogen receptor, larninin receptor, erb B and. . .

4.3 Combined Therapy with Immunotherapy, Traditional Chemo- or Radiotherapy

1.5 Tumor cell resistance to DNA damaging agents represents a major problem in clinical oncology. One goal of current cancer research is to find ways to improve the

efficacy of chemo- and radiotherapy. One way is by combining such traditional therapies with gene therapy. For example, the herpes simplex-thyraidine kinase (HS-tk) gene, when delivered to brain tumors by a retroviral vector system, successfully induced susceptibility to the antiviral agent ganciclovir (Culver et al., 1992). In the context of. . .

To HI cells, inhibit cell growth, inhibit metastasis, inhibit angiogenesis or otherwise reverse or reduce the malignant phenotype of tumor cells, using the methods and compositions of the present invention, one would generally contact a target cell with an BET expression construct. . .

I In treating cancer according to the invention, one would contact the tumor cells within agent in addition to the expression construct. This may be achieved by irradiating

<-----User Break----->

UV-light, γ -rays or even I O microwaves. Alternatively, the tumor cells may be contacted with the agent by administering to the subject a therapeutically effective amount of a pharmaceutical composition comprising a. . .

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(FILE 'HOME' ENTERED AT 08:51:47 ON 11 AUG 2005)

FILE 'PCTFULL' ENTERED AT 08:52:01 ON 11 AUG 2005

L1 268 S HYDROXYTAMOXIFEN OR (HYDRDROXY TAMOXIFEN)
L2 5061 S TAMOXIFEN
L3 67 S L2/AB
L4 25 S L2/TI
L5 5061 S L4 OR L2
L6 70 S L4 OR L3
L7 34444 S BREAST OR MAMMAR?
L8 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L9 2015 S L7/AB
L10 1529 S L9 AND L8
L11 57173 S PERCUTANEOUS? OR TOPICAL?
L12 498 S L11 AND L10
L13 10 S L12 AND L6
L14 5 S L13 AND L1
L15 1 S L14 NOT PY>2002

=> s l14 not py>2003
 184564 PY>2003
L16 2 L14 NOT PY>2003

=> d ibib 1

L16 ANSWER 1 OF 2 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2003039466 PCTFULL ED 20030520 EW 200320
TITLE (ENGLISH): METHOD OF TREATING OESTROGEN RESPONSIVE BREAST
 CANCER
TITLE (FRENCH): METHODE DE TRAITEMENT DU CANCER DU SEIN

INVENTOR(S) : REPDONDANT AUX OESTROGENES
 WONG, Grace, 100 Arlington Road, Brookline, MA 02467,
 US [CN, US];
 ESHKOL, Aliza, Ch. Du Petit Molard 1, CH-Ch-1278 La
 Rippe, CH [IL, CH];
 DELUCA, Giampiero, Chemin de la Florence 15, CH-1208
 Geneva, CH [IT, CH]

PATENT ASSIGNEE(S) : APPLIED RESEARCH SYSTEMS ARS HOLDING N.V., Pietermaai
 15, Curacao, AN [NL, NL], for all designates States
 except US;
 WONG, Grace, 100 Arlington Road, Brookline, MA 02467,
 US [CN, US], for US only;
 ESHKOL, Aliza, Ch. Du Petit Molard 1, CH-Ch-1278 La
 Rippe, CH [IL, CH], for US only;
 DELUCA, Giampiero, Chemin de la Florence 15, CH-1208
 Geneva, CH [IT, CH], for US only

AGENT: EISENSTEIN, Ronald, I.S., Nixon Peabody LLP, 101 Federal
 Street, Boston, MA 02110\$, US

LANGUAGE OF FILING: English
 LANGUAGE OF PUBL.: English
 DOCUMENT TYPE: Patent
 PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2003039466 | A2 | 20030515 |

DESIGNATED STATES
 W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR
 CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID
 IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD
 MG MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI
 SR SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW
 GH GM KE LS MW MZ SD SL SZ TZ UG ZM ZW
 RW (ARIGO): AM AZ BY KG KZ MD RU TJ TM
 RW (EAPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LU MC
 RW (EPO): NL PT SE SK TR
 RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG
 APPLICATION INFO.: WO 2002-US35438 A 20021105
 PRIORITY INFO.: US 2001-60/332,939 20011106

=> d ibib l14 1

L14 ANSWER 1 OF 5
 ACCESSION NUMBER: PCTFULL COPYRIGHT 2005 Univentio on STN
 2005058297 PCTFULL ED 20050706 EW 200526

TITLE (ENGLISH): USE OF 4-HYDROXYTAMOXIFEN FOR THE PREPARATION
 OF A MEDICAMENT FOR THE TREATMENT OF GYNECOMASTIA
 UTILISATION DE 4-HYDROXYTAMOXIFENE DANS LA PREPARATION
 D'UN MEDICAMENT DESTINE AU TRAITEMENT DE LA
 GYNECOMASTIE

INVENTOR(S) : LE NESTOUR, Elisabeth, 6, rue de Chaufourniers, F-75019
 Paris, FR [FR, FR];
 PALUMBO, Andrew, R., 7505 Colonial Road, Brooklyn, NY
 11209-2905, US [US, US]

PATENT ASSIGNEE(S) : LABORATOIRES BESINS INTERNATIONAL, 5, rue du Bourg
 l'Abbe, F-75003 Paris, FR [FR, FR], for all designates
 States except US;
 LE NESTOUR, Elisabeth, 6, rue de Chaufourniers, F-75019
 Paris, FR [FR, FR], for US only;
 PALUMBO, Andrew, R., 7505 Colonial Road, Brooklyn, NY
 11209-2905, US [US, US], for US only

AGENT: NARGOLWALLA, Cyra\$, Cabinet Plasseraud, 65/67, rue de
 la Victoire, F-75440 Paris Cedex 09\$, FR

LANGUAGE OF FILING:
LANGUAGE OF PUBL.:
DOCUMENT TYPE:
PATENT INFORMATION:

English
English
Patent

DESIGNATED STATES
W:

| NUMBER | KIND | DATE |
|---------------|------|----------|
| WO 2005058297 | A1 | 20050630 |

AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO
CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR
HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV
MA MD MG MK MN MW MX MZ NA NI NO NZ OM PG PH PL PT RO
RU SC SD SE SG SK SL SY TJ TM TN TR TT TZ UA UG US UZ
VC VN YU ZA ZM ZW

RW (ARIGO): BW GH GM KE LS MW MZ NA SD SL SZ TZ UG ZM ZW

RW (EAPO): AM AZ BY KG KZ MD RU TJ TM

RW (EPO): AT BE BG CH CY CZ DE DK EE ES FI FR GB GR HU IE IS IT
LT LU MC NL PL PT RO SE SI SK TR

RW (OAPI): BF BJ CF CG CI CM GA GN GQ GW ML MR NE SN TD TG

APPLICATION INFO.: WO 2004-EP14295 A 20041213
PRIORITY INFO.: EP 2003-03293156.0 20031215
US 2003-10/734,640 20031215

=> d his

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FILE 'PCTFULL' ENTERED AT 08:52:01 ON 11 AUG 2005

L1 268 S HYDROXYTAMOXIFEN OR (HYDRDROXY TAMOXIFEN)
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L5 5061 S L4 OR L2
L6 70 S L4 OR L3
L7 34444 S BREAST OR MAMMAR?
L8 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L9 2015 S L7/AB
L10 1529 S L9 AND L8
L11 57173 S PERCUTANEOUS? OR TOPICAL?
L12 498 S L11 AND L10
L13 10 S L12 AND L6
L14 5 S L13 AND L1
L15 1 S L14 NOT PY>2002
L16 2 S L14 NOT PY>2003

=> s l2 and l2
L17 5061 L2 AND L2

=> s l17 and l12
L18 145 L17 AND L12

=> s l2/clm
L19 752 (TAMOXIFEN/CLM)

=> s l1/clm
L20 29 HYDROXYTAMOXIFEN/CLM
3 HYRDRDROXY/CLM
752 TAMOXIFEN/CLM
0 HYDRDROXY TAMOXIFEN/CLM
((HYDRDROXY(W) TAMOXIFEN)/CLM)
29 (HYDROXYTAMOXIFEN/CLM OR (HYDRDROXY TAMOXIFEN/CLM))

=> s l20 or l19
L21 757 L20 OR L19

=> s l21 and l18
L22 36 L21 AND L18

=> s l22 not py>2002
294498 PY>2002
L23 16 L22 NOT PY>2002

=> s l23 not py>2001
398484 PY>2001
L24 15 L23 NOT PY>2001

=> d ibib 5

L24 ANSWER 5 OF 15 PCTFULL COPYRIGHT 2005 Univentio on STN
ACCESSION NUMBER: 2001054699 PCTFULL ED 20020827
TITLE (ENGLISH): SELECTIVE ESTROGEN RECEPTOR MODULATORS IN COMBINATION
WITH ESTROGENS
TITLE (FRENCH): MODULATEURS SELECTIFS DU RECEPTEUR D'OESTROGENE, EN
COMBINAISON AVEC DES OESTROGENES
INVENTOR(S): LABRIE, Fernand
PATENT ASSIGNEE(S): ENDORESCHERE, INC.;
LABRIE, Fernand
DOCUMENT TYPE: Patent
PATENT INFORMATION:

| | NUMBER | KIND | DATE |
|--------------------|--|------|----------|
| DESIGNATED STATES | WO 2001054699 | A1 | 20010802 |
| W: | AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU
CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN
IS JE KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK
MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM
TR TT TZ UA UG US UZ VN YU ZA ZW GH GM KE LS MW MZ SD
SL SZ TZ UG ZW AM AZ BY KG KZ MD RU TJ TM AT BE CH CY
DE DK ES FI FR GB GR IE IT LU MC NL PT SE TR BF BJ CF
CG CI CM GA GN GW ML MR NE SN TD TG | | |
| APPLICATION INFO.: | WO 2001-CA86 | A | 20010126 |
| PRIORITY INFO.: | US 2000-60/178,601 | | 20000128 |

=> d scan

L24 15 ANSWERS PCTFULL COPYRIGHT 2005 Univentio on STN
TIEN METHOD OF TREATMENT OF PROSTATE CANCER
TIFR METHODE DE TRAITEMENT DU CANCER DE LA PROSTATE

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2

L24 15 ANSWERS PCTFULL COPYRIGHT 2005 Univentio on STN
TIEN METHODS FOR IDENTIFYING, TREATING OR MONITORING ASYMPOTOMATIC PATIENTS
FOR RISK REDUCTION OR THERAPEUTIC TREATMENT OF BREAST CANCER
TIFR PROCEDES D'IDENTIFICATION, DE TRAITEMENT OU DE CONTROLE DES PATIENTS
ASYMPTOMATIQUES, POUR LA REDUCTION DES RISQUES OU LE TRAITEMENT
THERAPEUTIQUE DU CANCER DU SEIN

L24 15 ANSWERS PCTFULL COPYRIGHT 2005 Univentio on STN
TIEN BCMP-7 AS MARKER FOR DIAGNOSIS OF BREAST CANCER
TIFR BCMP 7 EN TANT QUE MARQUEUR POUR LE DIAGNOSTIC DU CANCER DU

SEIN

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):end

=> d his

(FILE 'HOME' ENTERED AT 08:51:47 ON 11 AUG 2005)

FILE 'PCTFULL' ENTERED AT 08:52:01 ON 11 AUG 2005
L1 268 S HYDROXYTAMOXIFEN OR (HYDRDROXY TAMOXIFEN)
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L6 70 S L4 OR L3
L7 34444 S BREAST OR MAMMAR?
L8 88096 S CANCER? OR TUMOR? OR NEOPLAS?
L9 2015 S L7/AB
L10 1529 S L9 AND L8
L11 57173 S PERCUTANEOUS? OR TOPICAL?
L12 498 S L11 AND L10
L13 10 S L12 AND L6
L14 5 S L13 AND L1
L15 1 S L14 NOT PY>2002
L16 2 S L14 NOT PY>2003
L17 5061 S L2 AND L2
L18 145 S L17 AND L12
L19 752 S L2/CLM
L20 29 S L1/CLM
L21 757 S L20 OR L19
L22 36 S L21 AND L18
L23 16 S L22 NOT PY>2002
L24 15 S L23 NOT PY>2001

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 21.54 | 21.75 |

STN INTERNATIONAL LOGOFF AT 09:00:36 ON 11 AUG 2005

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSSPTA1642BJF

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * * Welcome to STN International * * * * * * * * * * *

NEWS 1 Web Page for STN Seminar Schedule - N. America
NEWS 2 JUL 02 LMEDLINE coverage updated
NEWS 3 JUL 02 SCISEARCH enhanced with complete author names
NEWS 4 JUL 02 CHEMCATS accession numbers revised
NEWS 5 JUL 02 CA/Cplus enhanced with utility model patents from China
NEWS 6 JUL 16 Cplus enhanced with French and German abstracts
NEWS 7 JUL 18 CA/Cplus patent coverage enhanced
NEWS 8 JUL 26 USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 9 JUL 30 USGENE now available on STN
NEWS 10 AUG 06 CAS REGISTRY enhanced with new experimental property tags
NEWS 11 AUG 06 BEILSTEIN updated with new compounds
NEWS 12 AUG 06 FSTA enhanced with new thesaurus edition
NEWS 13 AUG 13 CA/Cplus enhanced with additional kind codes for granted patents
NEWS 14 AUG 20 CA/Cplus enhanced with CAS indexing in pre-1907 records
NEWS 15 AUG 27 Full-text patent databases enhanced with predefined patent family display formats from INPADOCDB
NEWS 16 AUG 27 USPATOLD now available on STN
NEWS 17 AUG 28 CAS REGISTRY enhanced with additional experimental spectral property data
NEWS 18 SEP 07 STN AnaVist, Version 2.0, now available with Derwent World Patents Index
NEWS 19 SEP 13 FORIS renamed to SOFIS
NEWS 20 SEP 13 INPADOCDB enhanced with monthly SDI frequency
NEWS 21 SEP 17 CA/Cplus enhanced with printed CA page images from 1967-1998
NEWS 22 SEP 17 Cplus coverage extended to include traditional medicine patents
NEWS 23 SEP 24 EMBASE, EMBAL, and LEMBASE reloaded with enhancements

NEWS EXPRESS 19 SEPTEMBER 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 19 SEPTEMBER 2007.

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NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8

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SINCE FILE TOTAL
ENTRY SESSION
0 21 0 21

FILE 'REGISTRY' ENTERED AT 07:08:40 ON 27 SEP 2007
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STRUCTURE FILE UPDATES: 26 SEP 2007 HIGHEST RN 948239-70-1
DICTIONARY FILE UPDATES: 26 SEP 2007 HIGHEST RN 948239-70-1

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/support/stngen/stndoc/properties.html>

```
=> s isopropyl myristate
    114659 ISOPROPYL
    2 ISOPROPYLS
    114659 ISOPROPYL
        (ISOPROPYL OR ISOPROPYLS)
    650 MYRISTATE
    3 MYRISTATES
    650 MYRISTATE
        (MYRISTATE OR MYRISTATES)
L1      5 ISOPROPYL MYRISTATE
        (ISOPROPYL(W)MYRISTATE)

=> s isopropyl myristate/cn
L2          1 ISOPROPYL MYRISTATE/CN

=> d cn

L2      ANSWER 1 OF 1  REGISTRY COPYRIGHT 2007 ACS on STN
CN      Tetradecanoic acid, 1-methylethyl ester (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN      Myristic acid, isopropyl ester (6CI, 7CI, 8CI)
OTHER NAMES:
CN      1-Methylethyl tetradecanoate
CN      Bisomel
CN      Crodadol IPM
CN      Crodamol IPM
CN      D 50
CN      D 50 (emollient)
CN      Deltyl Extra
CN      Emcol IM
CN      Emerest 2314
CN      Estol 1512
CN      Estol 1514
CN      Estol IPM 1512
CN      IPM
CN      IPM 100
```

CN IPM-EX
CN IPM-R
CN Isomyst
CN Isopropyl myristate
CN Isopropyl tetradecanoate
CN Kessco IPM
CN Kesscomir
CN Lexol IPM
CN Nikkol IPM
CN Nikkoi IPM 100
CN NSC 406280
CN Pelemol IPM
CN Promyr
CN Radia 7190
CN Rilanit IPM
CN Sinoester MIP
CN Stepan D 50
CN Stepan IPM
CN Tegosoft M
CN Wickenol 101

=> file caplus
COST IN U.S. DOLLARS

| | SINCE FILE | TOTAL |
|---------------------|------------|---------|
| | ENTRY | SESSION |
| FULL ESTIMATED COST | 18.15 | 18.36 |

FILE 'CPLUS' ENTERED AT 07:10:21 ON 27 SEP 2007
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FILE LAST UPDATED: 26 Sep 2007 (20070926/ED)

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They are available for your review at:

<http://www.cas.org/infpolicy.html>

=> s 12
L3 3572 L2

=> s percutaneous (L) 13
9742 PERCUTANEOUS
L4 75 PERCUTANEOUS (L) 13

=> s hydroxypropylcellulose/cn
REGISTRY INITIATED

Substance data SEARCH and crossover from CAS REGISTRY in progress...
Use DISPLAY HITSTR (or FHITSTR) to directly view retrieved structures.

L6 0 L5

=> s hydroxypropylcellulose
2579 HYDROXYPROPYLCCELLULOSE
5 HYDROXYPROPYLCCELLULOSES
L7 2581 HYDROXYPROPYLCCELLULOSE
(HYDROXYPROPYLCCELLULOSE OR HYDROXYPROPYLCCELLULOSES)

=> s 17 and 14
L8 0 L7 AND L4

=> s 14 not py>1999
8584294 PY>1999
L9 28 L4 NOT PY>1999

=> d ibib 1-5

L9 ANSWER 1 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:252431 CAPLUS
DOCUMENT NUMBER: 133:63806
TITLE: Influence of additives on percutaneous absorption of piroxicam from cataplasm
AUTHOR(S): Okuyama, Hirohisa; Ikeda, Yasuo; Imamori, Katsumi;
Takayama, Kozo; Nagai, Tsuneji
CORPORATE SOURCE: Central Res. Lab., SSP Co., Ltd., Narita, 286-8511,
Japan
SOURCE: Drug Delivery System (1999), 14(6), 491-497
CODEN: DDSYEI; ISSN: 0913-5006
PUBLISHER: Nippon DDS Gakkai Jimukyoku
DOCUMENT TYPE: Journal
LANGUAGE: Japanese

L9 ANSWER 2 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:780838 CAPLUS
DOCUMENT NUMBER: 130:257241
TITLE: Influence of propylene glycol and isopropyl myristate on the in vitro percutaneous penetration of diclofenac sodium from carbopol gels
AUTHOR(S): Arellano, A.; Santoyo, S.; Martin, C.; Ygartua, P.
CORPORATE SOURCE: Facultad de Farmacia, Departamento de Farmacia y
Tecnologia Farmaceutica, Universidad de Navarra,
Pamplona, 31080, Spain
SOURCE: European Journal of Pharmaceutical Sciences (1999),
7(2), 129-135
CODEN: EPSCED; ISSN: 0928-0987
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 3 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:459627 CAPLUS
DOCUMENT NUMBER: 129:280861
TITLE: Enhancement of percutaneous absorption of ketoprofen:

AUTHOR(S): effect of vehicles and adhesive matrix
Cho, Y.-J.; Choi, H.-K.
CORPORATE SOURCE: College of Pharmacy, Chosun University, Kwangju,
501-759, S. Korea
SOURCE: International Journal of Pharmaceutics (1998), 169(1),
95-104
PUBLISHER: CODEN: IJPHE; ISSN: 0378-5173
Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 4 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:430663 CAPLUS
DOCUMENT NUMBER: 129:86064
TITLE: Patches containing melatonin with good percutaneous
absorption and manufacture thereof
INVENTOR(S): Hidaka, Yoshifumi; Kato, Toshiyuki
PATENT ASSIGNEE(S): Teisan Seiyaku K. K., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 9 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|----------|
| JP 10182455 | A | 19980707 | JP 1996-343279 | 19961224 |
| PRIORITY APPLN. INFO.: | | | JP 1996-343279 | 19961224 |

L9 ANSWER 5 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1998:3676 CAPLUS
DOCUMENT NUMBER: 128:79882
TITLE: Influence of permeation enhancers on the in-vivo
percutaneous absorption of indomethacin
AUTHOR(S): Rao, P. Rama; Srinivas, V.; Diwan, Prakash V.
CORPORATE SOURCE: Pharmacology Division, Indian Institute Chemical
Technology, Hyderabad, 500 007, India
SOURCE: Eastern Pharmacist (1997), 40(476), 155-158
CODEN: EAPHA6; ISSN: 0012-8872
PUBLISHER: Eastern Pharmacist
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> d ibib 6-10

L9 ANSWER 6 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:790366 CAPLUS
DOCUMENT NUMBER: 128:93107
TITLE: Percutaneous absorption and histopathology of a
poloxamer-based formulation of capsaicin analog
AUTHOR(S): Lee, Beom-Jin; Lee, Tae-Sup; Cha, Bong-Jin; Kim,
Soon-Hoe; Kim, Won-Bae
CORPORATE SOURCE: College of Pharmacy, Biological Rhythm and Controlled
Release Laboratory, Kangwon National University,
Chuncheon, 200-701, S. Korea
SOURCE: International Journal of Pharmaceutics (1997), 159(1),

105-114
CODEN: IJPHDE; ISSN: 0378-5173
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:720069 CAPLUS
DOCUMENT NUMBER: 127:351231
TITLE: Alcoholic solutions containing acetylsalicylic acid for percutaneous administration in antithrombotic therapy
INVENTOR(S): Traus, Juergen; Teubner, Andreas; Wadenstorfer, Elmar
PATENT ASSIGNEE(S): Luitpold Pharma GmbH, Germany
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|------------|
| EP 803254 | A1 | 19971029 | EP 1997-106900 | 19970425 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| DE 19616539 | A1 | 19971106 | DE 1996-19616539 | 19960425 |
| CA 2199920 | A1 | 19971025 | CA 1997-2199920 | 19970313 |
| JP 10045599 | A | 19980217 | JP 1997-118630 | 19970423 |
| US 5900412 | A | 19990504 | US 1997-845386 | 19970425 |
| PRIORITY APPLN. INFO.: | | | DE 1996-19616539 | A 19960425 |

L9 ANSWER 8 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1997:641893 CAPLUS
DOCUMENT NUMBER: 127:283277
TITLE: Percutaneous absorption of LHRH through porcine skin: effect of N-methyl 2-pyrrolidone and isopropyl myristate
AUTHOR(S): Bhatia, K. S.; Singh, J.
CORPORATE SOURCE: Dep. Pharmaceutical Sci., Coll. Pharmacy, North Dakota State Univ., Fargo, ND, 58105, USA
SOURCE: Drug Development and Industrial Pharmacy (1997), 23(11), 1111-1114
CODEN: DDIPD8; ISSN: 0363-9045
PUBLISHER: Dekker
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 9 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1996:583214 CAPLUS
DOCUMENT NUMBER: 125:308799
TITLE: In vitro percutaneous absorption of piroxicam through synthetic membranes and abdominal rat skin
AUTHOR(S): Santoyo, S.; Arellano, A.; Ygartua, P.; Martin, C.
CORPORATE SOURCE: Departamento de Farmacia y Tecnología Farmacéutica, Facultad de Farmacia, Universidad de Navarra, Apt. 273, Pamplona, 31080, Spain
SOURCE: Pharmaceutica Acta Helveticae (1996), 71(2), 141-146

CODEN: PAHEAA; ISSN: 0031-6865
 PUBLISHER: Elsevier
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 L9 ANSWER 10 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1995:986597 CAPLUS
 DOCUMENT NUMBER: 124:15517
 TITLE: Percutaneous pharmaceutical preparations containing buprenorphine
 INVENTOR(S): Tokuda, Shoichi; Ninomiya, Kazuhisa; Fukushima, Yasuhiro; Watanabe, Shigeyuki; Ochiai, Mitsuru; Okumura, Mutsuo; Hosokawa, Yuko
 PATENT ASSIGNEE(S): Nitto Denko Corp., Japan; Nikken Chemicals Co., Ltd.
 SOURCE: Eur. Pat. Appl., 33 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 680754 | A2 | 19951108 | EP 1995-106861 | 19950505 |
| EP 680754 | A3 | 19960306 | | |
| EP 680754 | B1 | 19980930 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE | | | | |
| JP 07304672 | A | 19951121 | JP 1994-94241 | 19940506 |
| JP 2819236 | B2 | 19981030 | | |
| CA 2147918 | A1 | 19951107 | CA 1995-2147918 | 19950426 |
| AT 171619 | T | 19981015 | AT 1995-106861 | 19950505 |
| ES 2123177 | T3 | 19990101 | ES 1995-106861 | 19950505 |
| CN 1116525 | A | 19960214 | CN 1995-107104 | 19950506 |
| PRIORITY APPLN. INFO.: | | | JP 1994-94241 | A 19940506 |

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L9 ANSWER 7 OF 28 CAPLUS COPYRIGHT 2007 ACS on STN
 IT 67-63-0, Isopropanol, biological studies 105-99-7, Butyl adipate
 110-27-0, Isopropyl myristate 6938-94-9, Isopropyl adipate
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (alc. solns. containing acetylsalicylic acid for percutaneous administration in antithrombotic therapy)

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|----------------------|------------------|---------------|
| FULL ESTIMATED COST | 18.51 | 45.22 |

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 26 SEP 2007 HIGHEST RN 948239-70-1
 DICTIONARY FILE UPDATES: 26 SEP 2007 HIGHEST RN 948239-70-1

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<http://www.cas.org/support/stngen/stndoc/properties.html>

=> E "HYDROXYPROPYL CELLULOSE"/CN 25
E1 1 HYDROXYPROPYL CELLULOSE-METHYL METHACRYLATE GRAFT COPOLYMER/CN
E2 1 HYDROXYPROPYL CELLULOSE-VINYLPHOSPHONIC ACID GRAFT COPOLYMER/CN
E3 0 --> HYDROXYPROPYL CELLULOSE/CN
E4 1 HYDROXYPROPYL CHITOSAN/CN
E5 1 HYDROXYPROPYL CHITOSAN ACETATE/CN
E6 1 HYDROXYPROPYL CHITOSAN-METHACRYLIC ACID GRAFT COPOLYMER/CN
E7 1 HYDROXYPROPYL CYANOCELLULOSE/CN
E8 1 HYDROXYPROPYL DEXTRIN/CN
E9 1 HYDROXYPROPYL DEXTRIN SUCCINATE/CN
E10 1 HYDROXYPROPYL DISTARCH PHOSPHATE/CN
E11 1 HYDROXYPROPYL ETHER OF CELLULOSE/CN
E12 1 HYDROXYPROPYL ETHYL CELLULOSE/CN
E13 1 HYDROXYPROPYL ETHYL CELLULOSE PHTHALATE/CN
E14 1 HYDROXYPROPYL ETHYL MALEATE/CN
E15 1 HYDROXYPROPYL ETHYLBENZOIC ACID CELLULOSE ACETATE/CN
E16 1 HYDROXYPROPYL GROUP-CONTG. DI-ME SILOXANES/CN
E17 1 HYDROXYPROPYL GROUP-TERMINATED DI-ME SILOXANES/CN
E18 1 HYDROXYPROPYL GROUP-TERMINATED SILOXANES AND SILICONES/CN
E19 1 HYDROXYPROPYL GUAR/CN
E20 1 HYDROXYPROPYL GUAR GUM/CN
E21 1 HYDROXYPROPYL GUAR GUM ETHER WITH GLYCIDYLTRIMETHYLAMMONIUM CHLORIDE/CN
E22 1 HYDROXYPROPYL GUAR GUM STEARATE ESTER/CN
E23 1 HYDROXYPROPYL GUAR HYDROXYPROPYLTRIMONIUM CHLORIDE/CN
E24 1 HYDROXYPROPYL GUAR PALMITATE ESTER/CN
E25 1 HYDROXYPROPYL GUAR STEARATE/CN

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E4 1 HYDROXYPROPYL CELLULOSE ACETATE/CN
E5 1 HYDROXYPROPYL CELLULOSE ACETATE PHTHALATE/CN
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E7 1 HYDROXYPROPYL CELLULOSE ACETATE SUCCINATE/CN
E8 1 HYDROXYPROPYL CELLULOSE ACETATE SUCCINATE TRIMELLITATE/CN
E9 1 HYDROXYPROPYL CELLULOSE ACETATE TRIMELLITATE/CN
E10 1 HYDROXYPROPYL CELLULOSE ACETATE TRIMELLITATE SUCCINATE/CN
E11 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE/CN
E12 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE HOMOPOLYMER/CN
E13 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE-KAYRAD DPMA
COPOLYMER/CN
E14 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE-KAYRAD PEG 400DA
COPOLYMER/CN
E15 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE-KAYRAD PET 301
COPOLYMER/CN
E16 1 HYDROXYPROPYL CELLULOSE ACRYLATE BUTYRATE-KAYRAD RM 1001
COPOLYMER/CN

E17 1 HYDROXYPROPYL CELLULOSE ACRYLATE PROPIONATE-KAYARAD R 167
COPOLYMER/CN
E18 1 HYDROXYPROPYL CELLULOSE BENZOATE/CN
E19 1 HYDROXYPROPYL CELLULOSE BUTYRATE/CN
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E23 1 HYDROXYPROPYL CELLULOSE HYDROGEN PHOSPHONATE/CN
E24 1 HYDROXYPROPYL CELLULOSE ISOBUTYRATE/CN
E25 1 HYDROXYPROPYL CELLULOSE ISOVALERATE/CN

=> S E3
L10 1 "HYDROXYPROPYL CELLULOSE"/CN

=> file caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
ENTRY SESSION
FULL ESTIMATED COST 5.85 51.07

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FILE COVERS 1907 - 27 Sep 2007 VOL 147 ISS 14
FILE LAST UPDATED: 26 Sep 2007 (20070926/ED)

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FILE 'REGISTRY' ENTERED AT 07:08:40 ON 27 SEP 2007
L1 5 S ISOPROPYL MYRISTATE
L2 1 S ISOPROPYL MYRISTATE/CN

FILE 'CAPLUS' ENTERED AT 07:10:21 ON 27 SEP 2007
L3 3572 S L2
L4 75 S PERCUTANEOUS (L) L3
S HYDROXYPROPYLCELLULOSE/CN

FILE 'REGISTRY' ENTERED AT 07:11:15 ON 27 SEP 2007
L5 0 S HYDROXYPROPYLCELLULOSE/CN

FILE 'CAPLUS' ENTERED AT 07:11:16 ON 27 SEP 2007
L6 0 S L5
L7 2581 S HYDROXYPROPYLCELLULOSE

L8 0 S L7 AND L4
L9 28 S L4 NOT PY>1999

FILE 'REGISTRY' ENTERED AT 07:14:11 ON 27 SEP 2007
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E "HYDROXYPROPYL CELLULOSE"/CN 25

L10 1 S E3

FILE 'CAPLUS' ENTERED AT 07:15:07 ON 27 SEP 2007

=> s l10
L11 11350 L10

=> s l11 and l3
L12 142 L11 AND L3

=> s l11 and l4
L13 1 L11 AND L4

=> d ibib

L13 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2006:888111 CAPLUS
DOCUMENT NUMBER: 145:256238
TITLE: Adhesive gels containing acid anhydride copolymers and polyhydric alcohols
INVENTOR(S): Nihei, Tomoya; Unagami, Runa; Matsuda, Kazuhiko;
Yamagata, Yoshifumi; Gotoh, Hajime; Asanuma, Takeyuki;
Tagaki, Narumi; Sakamoto, Yasunori
PATENT ASSIGNEE(S): Lion Corporation, Japan
SOURCE: PCT Int. Appl., 34pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|--|------------------|------------|
| WO 2006090824 | A1 | 20060831 | WO 2006-JP303391 | 20060224 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KM, KN, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ,
NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN,
YU, ZA, ZM, ZW | | | | |
| RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE,
IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ,
CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM | | | | |
| JP 2006232724 | A | 20060907 | JP 2005-49347 | 20050224 |
| PRIORITY APPLN. INFO.: | | | JP 2005-49347 | A 20050224 |
| OTHER SOURCE(S): | MARPAT | 145:256238 | | |
| REFERENCE COUNT: | 19 | THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT | | |

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FILE 'REGISTRY' ENTERED AT 07:08:40 ON 27 SEP 2007
 L1 5 S ISOPROPYL MYRISTATE
 L2 1 S ISOPROPYL MYRISTATE/CN

 FILE 'CAPLUS' ENTERED AT 07:10:21 ON 27 SEP 2007
 L3 3572 S L2
 L4 75 S PERCUTANEOUS (L) L3
 S HYDROXYPROPYLCELLULOSE/CN

 FILE 'REGISTRY' ENTERED AT 07:11:15 ON 27 SEP 2007
 L5 0 S HYDROXYPROPYLCELLULOSE/CN

 FILE 'CAPLUS' ENTERED AT 07:11:16 ON 27 SEP 2007
 L6 0 S L5
 L7 2581 S HYDROXYPROPYLCELLULOSE
 L8 0 S L7 AND L4
 L9 28 S L4 NOT PY>1999

 FILE 'REGISTRY' ENTERED AT 07:14:11 ON 27 SEP 2007
 E "HYDROXYPROPYL CELLULOSE"/CN 25
 E "HYDROXYPROPYL CELLULOSE"/CN 25
 L10 1 S E3

 FILE 'CAPLUS' ENTERED AT 07:15:07 ON 27 SEP 2007
 L11 11350 S L10
 L12 142 S L11 AND L3
 L13 1 S L11 AND L4

 => s percutaneous
 L14 9742 PERCUTANEOUS

 => s l14 and l12
 L15 10 L14 AND L12

 => s l15 not py>1999
 8584294 PY>1999
 L16 1 L15 NOT PY>1999

 => d ibib

 L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
 ACCESSION NUMBER: 1985:583579 CAPLUS
 DOCUMENT NUMBER: 103:183579
 TITLE: Pharmaceutical for percutaneous application
 of metoclopramide
 INVENTOR(S): Saito, Kenichiro; Heller, Jorge; Skinner, Wilfred A.
 PATENT ASSIGNEE(S): Nitto Electric Industrial Co., Ltd. , Japan
 SOURCE: Ger. Offen., 28 pp.
 CODEN: GWXXBX
 DOCUMENT TYPE: Patent
 LANGUAGE: German
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|-------------|------|----------|-----------------|----------|
| DE 3503279 | A1 | 19850808 | DE 1985-3503279 | 19850131 |
| DE 3503279 | C2 | 19890309 | | |
| US 4605670 | A | 19860812 | US 1984-576087 | 19840201 |
| JP 60161918 | A | 19850823 | JP 1984-175206 | 19840824 |
| SE 8405929 | A | 19850802 | SE 1984-5929 | 19841123 |

| | | | | |
|------------------------|--------|------------|----------------|------------|
| SE 465452 | B | 19910916 | | |
| SE 465452 | C | 19920123 | | |
| NL 8403618 | A | 19850902 | NL 1984-3618 | 19841128 |
| CA 1252049 | A1 | 19890404 | CA 1984-468965 | 19841129 |
| GB 2153223 | A | 19850821 | GB 1984-30458 | 19841203 |
| GB 2153223 | B | 19870624 | | |
| DK 8500433 | A | 19850802 | DK 1985-433 | 19850131 |
| CH 667810 | A5 | 19881115 | CH 1985-439 | 19850131 |
| FR 2558729 | A1 | 19850802 | FR 1985-1459 | 19850201 |
| FR 2558729 | B1 | 19881028 | | |
| PRIORITY APPLN. INFO.: | | | US 1984-576087 | A 19840201 |
| OTHER SOURCE(S): | MARPAT | 103:183579 | | |

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L16 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2007 ACS on STN
 TI Pharmaceutical for percutaneous application of metoclopramide
 AB Metoclopramide (I) [364-62-5], for percutaneous administration,
 is incorporated into a carrier system containing monovalent aliphatic C6-24
 alcs.
 and/or esters of monovalent alcs. with C8-32 monocarboxylic. . .
 IT 57-55-6, biological studies 513-85-9 9004-62-0 9004-64-2
 RL: BIOL (Biological study)
 (metoclopramide absorption by skin from pharmaceuticals containing alcs. or
 esters and lactams and)
 IT 78-70-6 106-32-1 110-27-0 111-87-5, biological studies
 112-53-8 143-28-2 150-86-7 515-69-5 589-62-8 3234-85-3
 3687-46-5 5333-42-6 58670-89-6
 RL: BIOL (Biological study)
 (metoclopramide absorption by skin from pharmaceuticals containing lactams
 and)

=>

---Logging off of STN---

=>

Executing the logoff script...

=> LOG Y

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 9.78 | 60.85 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | -0.78 | -0.78 |

STN INTERNATIONAL LOGOFF AT 07:17:10 ON 27 SEP 2007